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Agios Data Update at ASH

December 4, 2016

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 pyruvate kinase-R mutations as therapeutic targets; the potential benefits of its product candidates targeting IDH1/IDH2 or pyruvate kinase-R mutations, including enasidenib (AG-221), AG-120, AG-348 and AG-519; its plans and timelines for the further clinical development of AG-120, AG-348 and AG-519; potential NDA submissions for enasidenib (AG-221) and/or AG-120; and 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; that positive safety and efficacy findings observed in early stage clinical trials will be replicated in later stage trials; that a submitted NDA will be accepted; that an accepted NDA will be approved; 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' public filings with the Securities and Exchange Commission. 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.

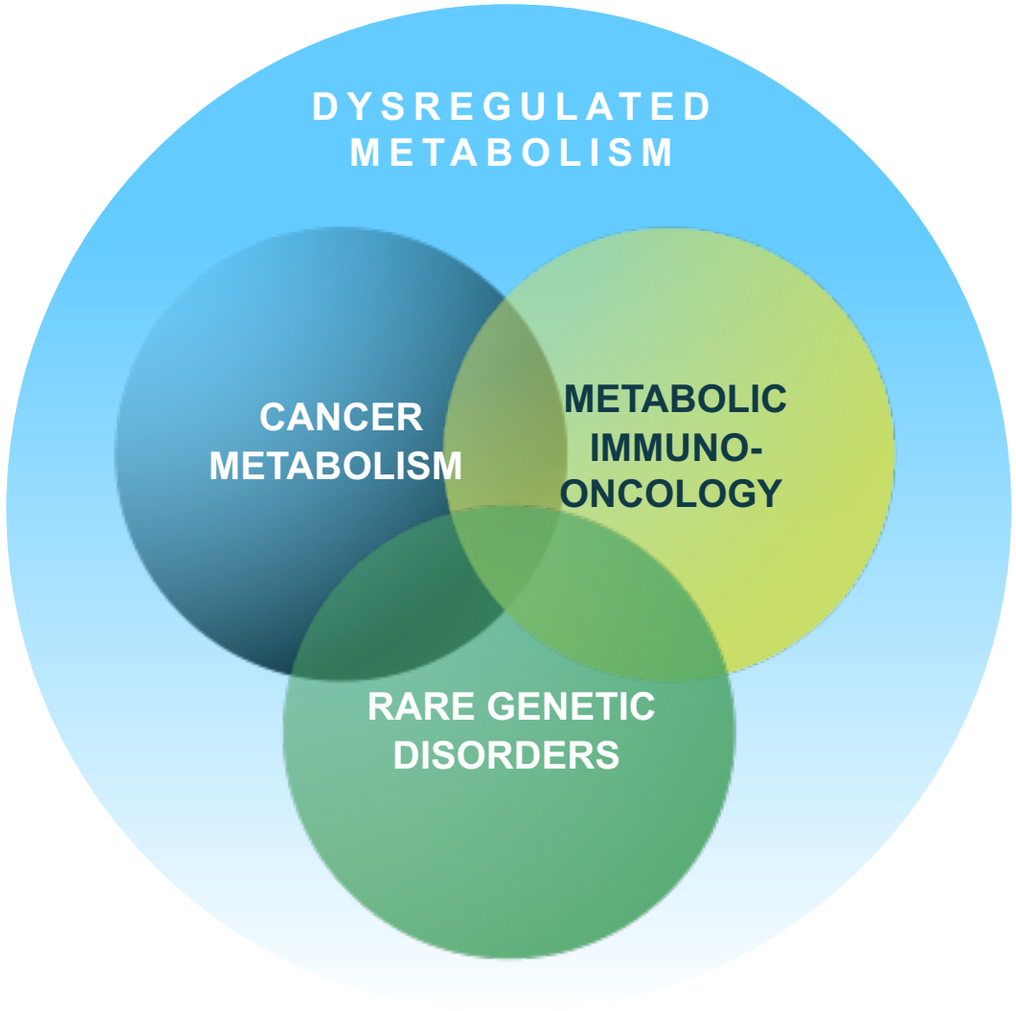
Today's Agenda

- Our Vision and Science – **David Schenkein, M.D.**
- AG-348 Data Update and PK Deficiency Review – **Rachael Grace, M.D., Dana-Farber Boston Children's Cancer and Blood Disorder Center**
- AG-519 Data Review – **Chris Bowden, M.D.**
- AML Landscape – **Eytan Stein, M.D., Memorial Sloan Kettering Cancer Center**
- Closing Remarks – **David Schenkein**
- Q&A – **Rachael Grace, Eytan Stein, David Schenkein, Chris Bowden & Scott Biller, Ph.D.**

Our Vision and Science

David Schenkein, M.D.
Chief Executive Officer

We Are Driven By a Clear Vision and Values



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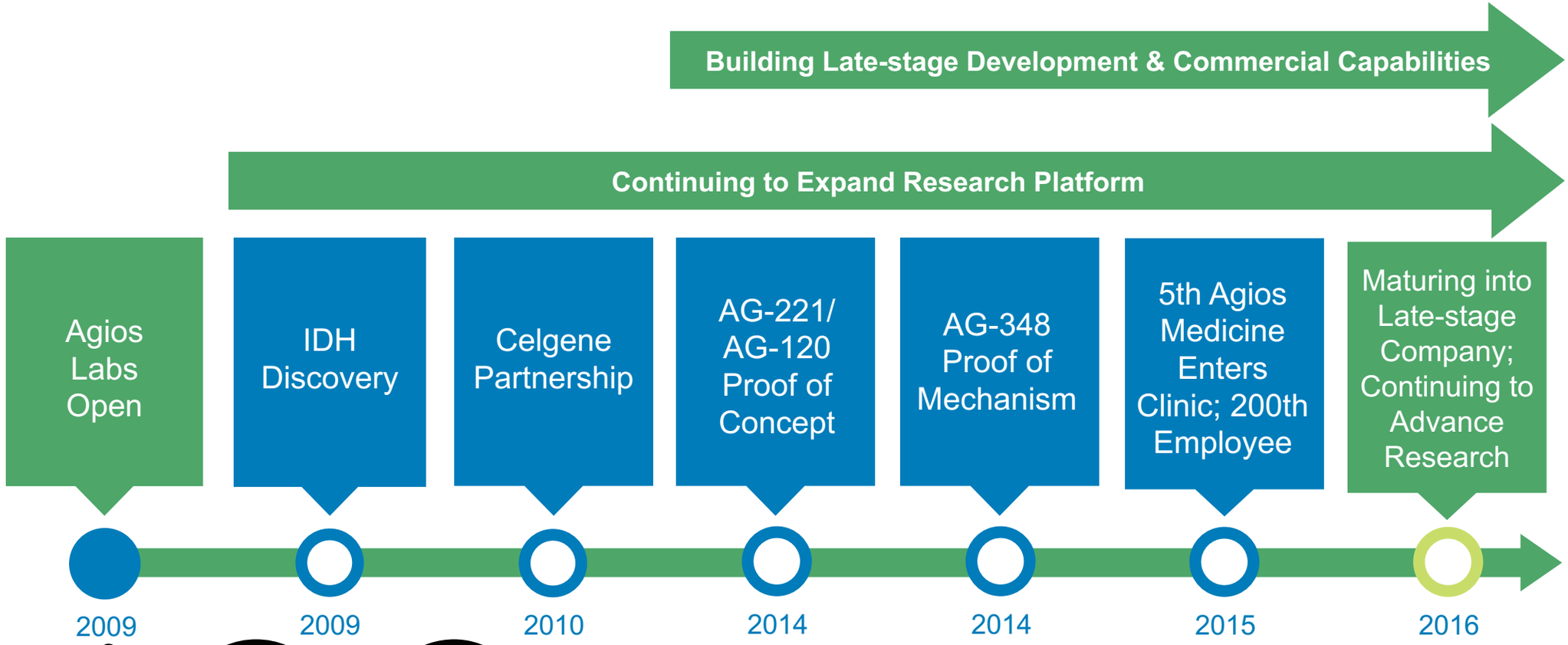
Agios is passionately committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and rare genetic disorders.

Building a Great Sustainable Biopharmaceutical Company



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2016 ASH Presentations

Topic/Date	Title	No.
AG-348 DRIVE PK – Oral Sun., Dec. 4, 5:45-6:00pm (4:30-6pm session)	Effects of AG-348, a Pyruvate Kinase Activator, on Anemia and Hemolysis in Patients With Pyruvate Kinase Deficiency: Data From the DRIVE PK Study	402
AG-120 Clinical – Oral Mon., Dec. 5, 4:45-5:00pm (4:30-6pm session)	Determination of IDH1 Mutational Burden and Clearance via Next-Generation Sequencing in Patients With IDH1 Mutation-Positive Hematologic Malignancies Receiving AG-120, a First-in-Class Inhibitor of Mutant IDH1	1070
AG-221 MDS – Oral Sun., Dec. 4, 9:30-9:45am (9:30-11am session)	Enasidenib (AG-221), a Potent Oral Inhibitor of Mutant Isocitrate Dehydrogenase 2 (IDH2) Enzyme, Induces Hematologic Responses in Patients with Myelodysplastic Syndromes (MDS)	343
AG-519 Clinical – Poster Sat., Dec. 3, 5:30-7:30pm	Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Multiple Doses of AG-519, an Allosteric Activator of Pyruvate Kinase-R, in Healthy Subjects	1264
AG-348 RBC Metabolism – Poster Sun., Dec. 4, 6:00-8:00pm	Characterization of Metabolic Response to AG-348, an Allosteric Activator of Red Cell Pyruvate Kinase, in Healthy Volunteers and Pyruvate Kinase Deficiency Patients	2452
AG-519 PK/PD – Poster Sat., Dec. 3, 5:30-7:30pm	Population Pharmacokinetics and Pharmacodynamics of AG-519, a Pyruvate Kinase Activator for the Treatment of Pyruvate Kinase Deficiency, in Human Healthy Volunteers	1263
NHS Iron Overload – Poster Sun., Dec. 4, 6:00-8:00pm	Iron Overload is Highly Prevalent in All Disease Severity States in Pyruvate Kinase Deficiency (PKD)	2430

Today's PKR Key Takeaways

- Updated DRIVE PK data continue to demonstrate clinically meaningful impact on hemoglobin with additional patients and longer follow-up
  - Robust, rapid and sustained increases in hemoglobin (15/32 patients overall; 15/26 with at least one missense mutation)
    - Continuing to evaluate genotype/response relationship
  - Well-tolerated safety profile, up to six months of twice daily dosing
    - Clinical significance of aromatase inhibition remains unclear
  - First metabolic data linking increases in hemoglobin with increased PKR pathway function
- Clear proof-of-mechanism for AG-519, with activity comparable to that of AG-348
  - Well-tolerated, up to 14 days of twice daily dosing
  - Robust dose-dependent changes in ATP and 2,3-DPG blood levels
- Program heading into pivotal development

Today's IDH Key Takeaways

- Executing late-stage clinical development for enasidenib and AG-120
  - Enasidenib (AG-221) on track for NDA submission in IDH2m positive R/R AML by year end
  - Plan to explore similar expedited regulatory strategy for AG-120; could result in 2017 NDA submission

- Updated Phase 1 dose-escalation data in abstract confirm AG-120's robust, durable clinical activity as a single agent
  - 38% ORR (30/78) and 18% CR (14/78)

- First demonstration that AG-120 changes the biology of disease through mutational clearance of IDH1

The Biology and Burden of PK Deficiency

Rachael Grace, M.D.
Dana-Farber Boston Children's Cancer
and Blood Disorder Center

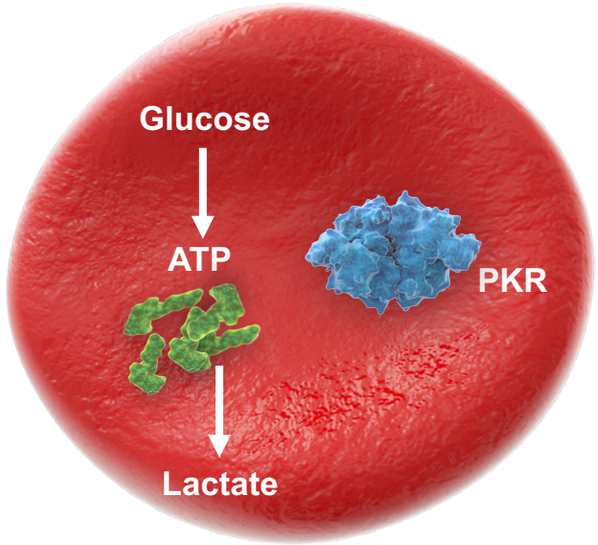
PK Deficiency Is a Rare Genetic Disease that Affects Red Blood Cells

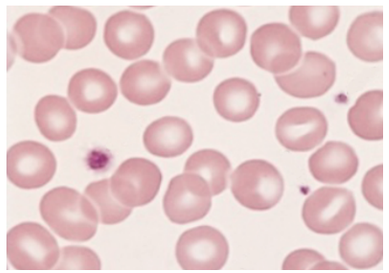
Rare genetic disease of erythrocyte pyruvate kinase

- PK deficiency often presents at birth with jaundice and can cause lifelong hemolytic anemia and associated morbidities.
- Estimated prevalence ranges from ~1:20K to ~1:485K[1–4]

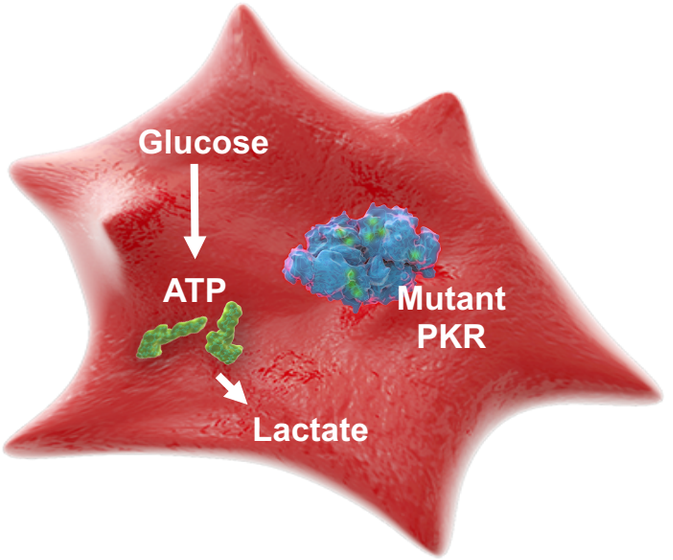
PKR regulates a crucial step in red blood cell metabolism and when mutated causes premature death of these cells

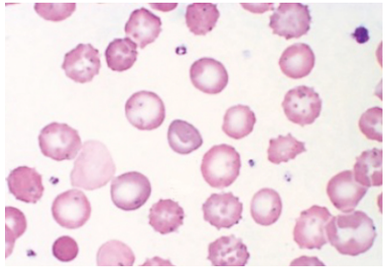
Healthy





PK Deficiency





Grace R et al. *Am J Hematol* 2015;90(9):825-30; [1]Mohrenweiser HW *PNAS* 1981;78(8):5046-50; [2]Carey PJ et al. *Blood* 2000;96(12):4005-6; [3]Beutler E & Gelbart T *Blood* 2000;95(11):3585-8; [4]deMedicis et al. *Hum Hered* 1992;42(3):179-83

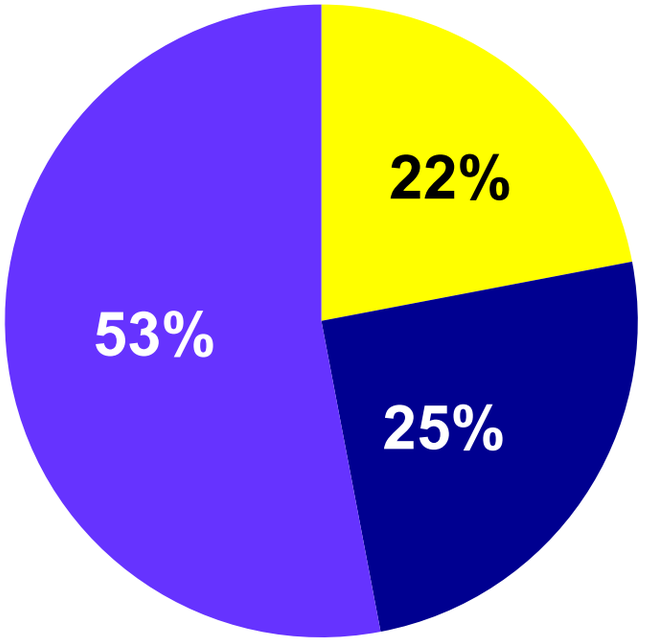
Over 250 Mutations Cause a Range of Defective PKR Proteins

Over 250 mutations in PKR have been described in PK deficiency, belonging to one of two categories:

1. **Missense mutations** cause a single amino acid change in the protein – *generally some functional protein*

2. **Non-missense mutation** any mutation other than a missense mutation (*e.g.*, stop, frameshift, deletion) – *generally little functional protein*

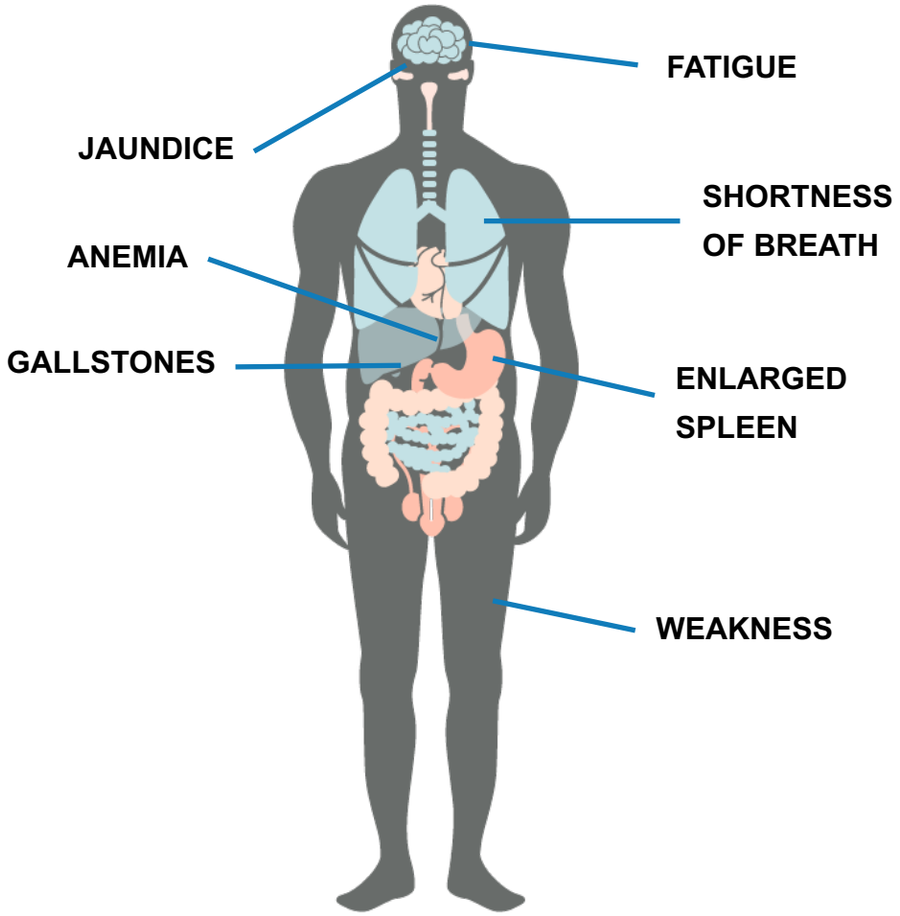
Type of PKR mutations found in 74 unrelated PK deficiency cases enrolled in the natural history study



Sources: R van Wijk, Blood 2005; P Bianchi, poster ASH 2015

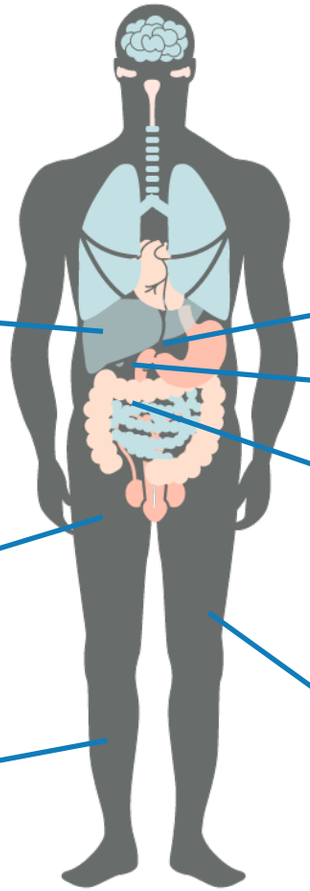
PK Deficiency Is a Lifelong Disease with Only Supportive Treatments

Lifelong Symptoms



	Supportive Treatments	Complications
INFANT	• Phototherapy • Blood transfusions	
CHILD	• Removal of spleen • Removal of gall bladder • Blood transfusions	• Infection risk → lifelong prophylactic antibiotics • Thrombosis risk
ADULT	• Blood transfusions	• Iron overload → iron chelation therapy

Clearer Picture of Disease Burden Already Emerging with Help from the Natural History Study



IRON CHELATION (24%)

GALLSTONES (42%)

GALL BLADDER REMOVAL (37%)

SPLEEN REMOVAL (68%)

RBC PRODUCTION IN INAPPROPRIATE ORGANS (14%)

DECREASED BONE STRENGTH (6%)

APLASTIC CRISIS (16%)

BLOOD CLOTS (5%)

Baseline and retrospective data from 144 NHS patients | Source : R. Grace, poster ASH 2015

PKR Mechanism

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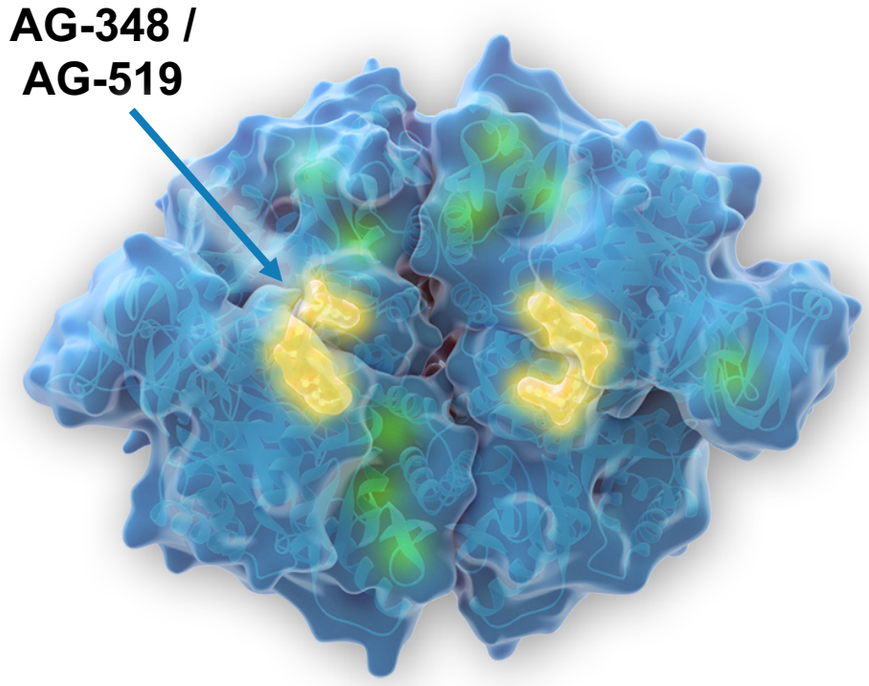
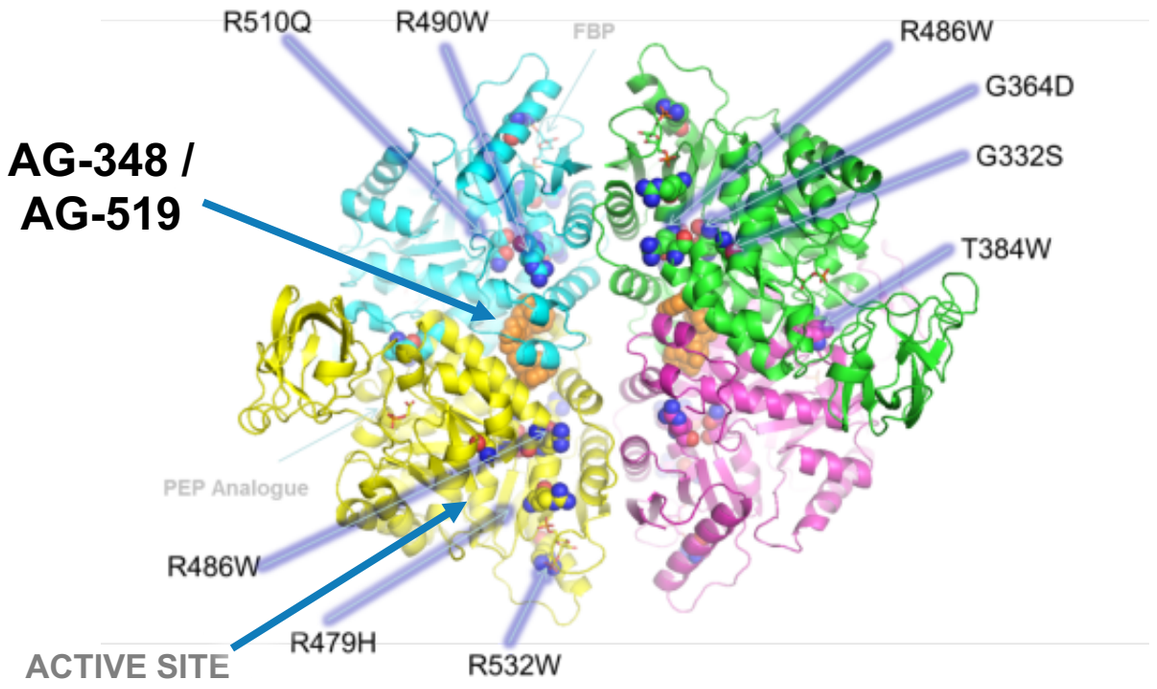
AG-348 and AG-519 Activate a Wide Variety of Mutant PKR Enzymes

PKR is a protein with four subunits (tetramer)



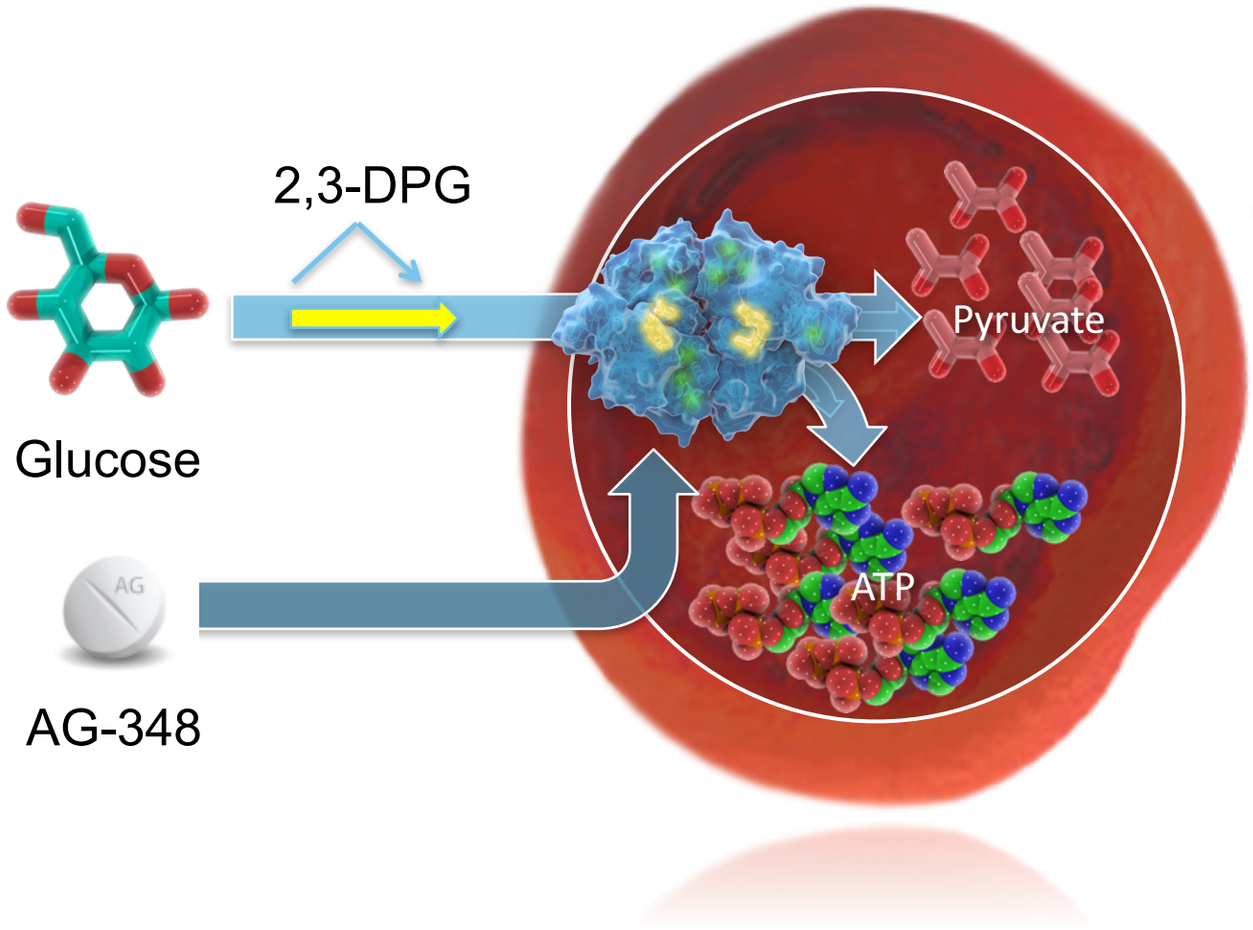
AG-348 and AG-519 bind at the dimer-dimer interface

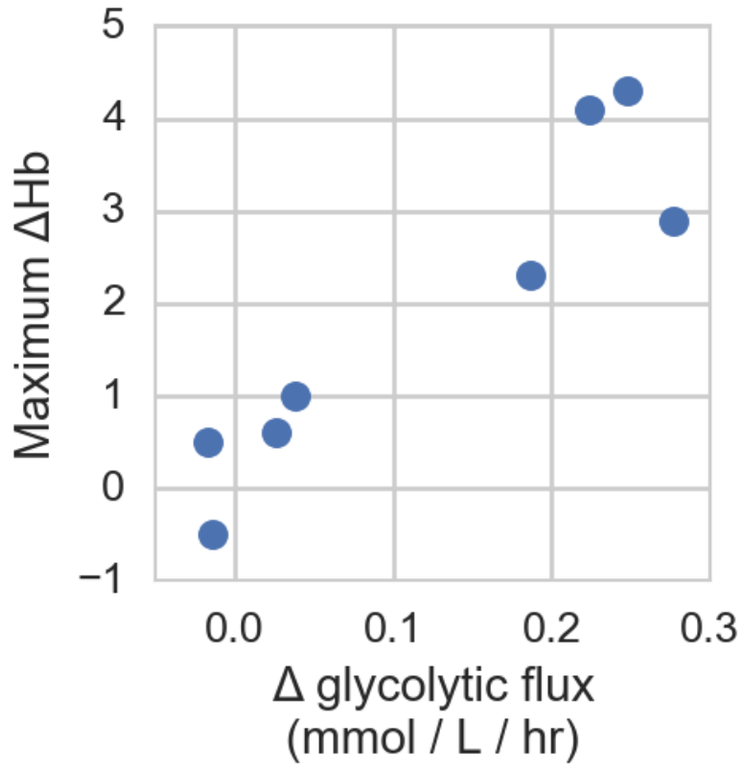
Common PKR mutations



AG-348 and AG-519 bind away from common mutations

First Data Linking AG-348's Impact on Hemoglobin With PKR Pathway Activation





Patients with Hb increases of >1.0 g/dL experienced a >50% average increase in the rate of metabolism of the PKR pathway

Review of DRIVE PK Findings

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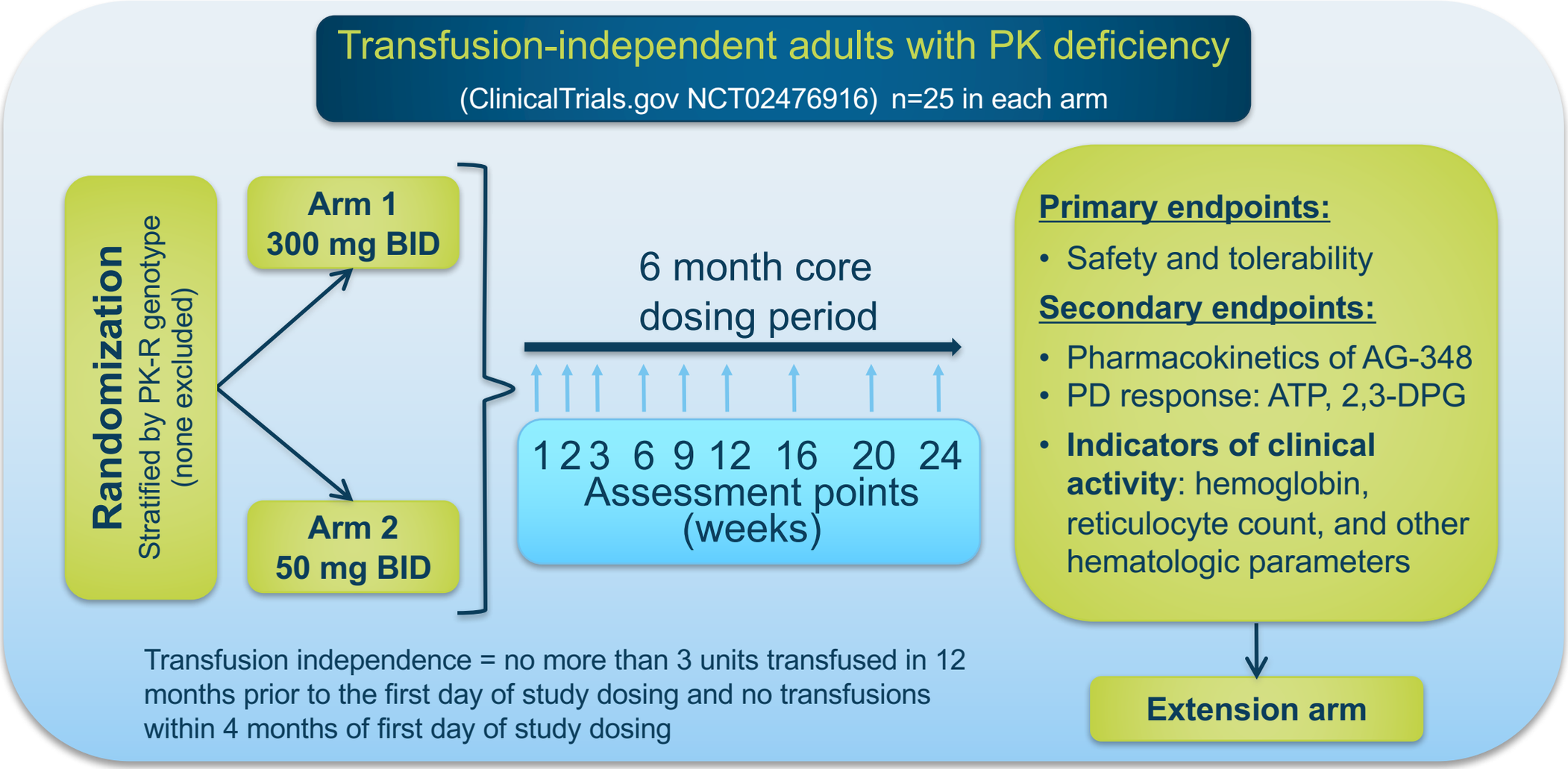
Study Design

DRIVEPK

Open-label, global Phase 2 study: 14 centers in the U.S., Canada and EU



Demographics and Disposition

- Study initiated June 2015; data cut-off September 23, 2016
- Evaluable analysis set: ≥3 weeks of data (n=32)
- Safety analysis set: received at least 1 dose of AG-348 (n=34)
- 13 patients ongoing in the core period (as of September 23, 2016)
  - Early discontinuations in the core period due to: relocation (n=1), AEs (n=3)
- Of the 17 patients who completed the core period, 15 enrolled in the extension period
- 1 patient discontinued in extension period due to physician decision (lack of efficacy)

Characteristics	50 mg BID, n=17	300 mg BID, n=17	Total, N=34
Men/women, n	11/6	9/8	20/14
Age in years, mean (range)	28.5 (19-45)	37.0 (20-61)	32.8 (19-61)
Race[a] white, n	15	15	30
Hemoglobin (Hb) baseline, g/dL, mean (SD, range)	9.8 (1.41, 7.6–12.4)	8.7 (1.37, 6.5–11.8)	9.2 (1.47, 6.5–12.4)
Duration of treatment, weeks, median (range)	24.7 (4.7–50.4)	24.0 (2.4–44.4)	24.4 (2.4–50.4)
Splenectomized, n	14	14	28

 Data presented at ASH 2016, 12/4

[a]Not reported in 2 patients, 2 patients were Asian; AE = adverse event; SD = standard deviation

Safety Summary

- AG-348 was generally well tolerated; the majority of AEs were grade 1–2
  - No grade 4 AEs or deaths
  - 2 patients experienced serious AEs: Grade 2 osteoporosis; hemolysis and anemia due to discontinuation of the drug after a rapid Hb response (patient continued in the study)
  - 3 patients discontinued treatment due to AEs
  - DXA scan data (n=17) show high variability and are inconclusive

AEs, regardless of causality (occurring in >5 patients or assessed as Grade ≥3)	50 mg BID n=17		300 mg BID n=17		Total N=34	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Patients experiencing at least 1 AE, n	13	2	17	6	30	8
Headache	7	0	8	0	15	0
Nausea	7	0	7	0	14	0
Insomnia	3	1	10	1	13	2
Fatigue	3	0	3	0	6	0
Vomiting	2	0	4	0	6	0
Hypertriglyceridemia	0	0	4	3	4	3
Anaemia	1	1[a]	1	1[b]	2	2
Hypertension	0	0	1	1	1	1
Dizziness	2	0	1	1	3	1
Haemolysis	0	0	2	1[b]	2	1

[a]Grade 3 anemia, not a serious AE. [b]Grade 3 withdrawal hemolysis and anemia in 46-year-old woman due to abrupt drug withdrawal after a very fast Hb response
AEs were graded using National Cancer Institute Common Terminology Criteria, version 4.03. Hb = hemoglobin; DXA = Dual energy X-ray absorptiometry
Data presented at ASH 2016, 12/4

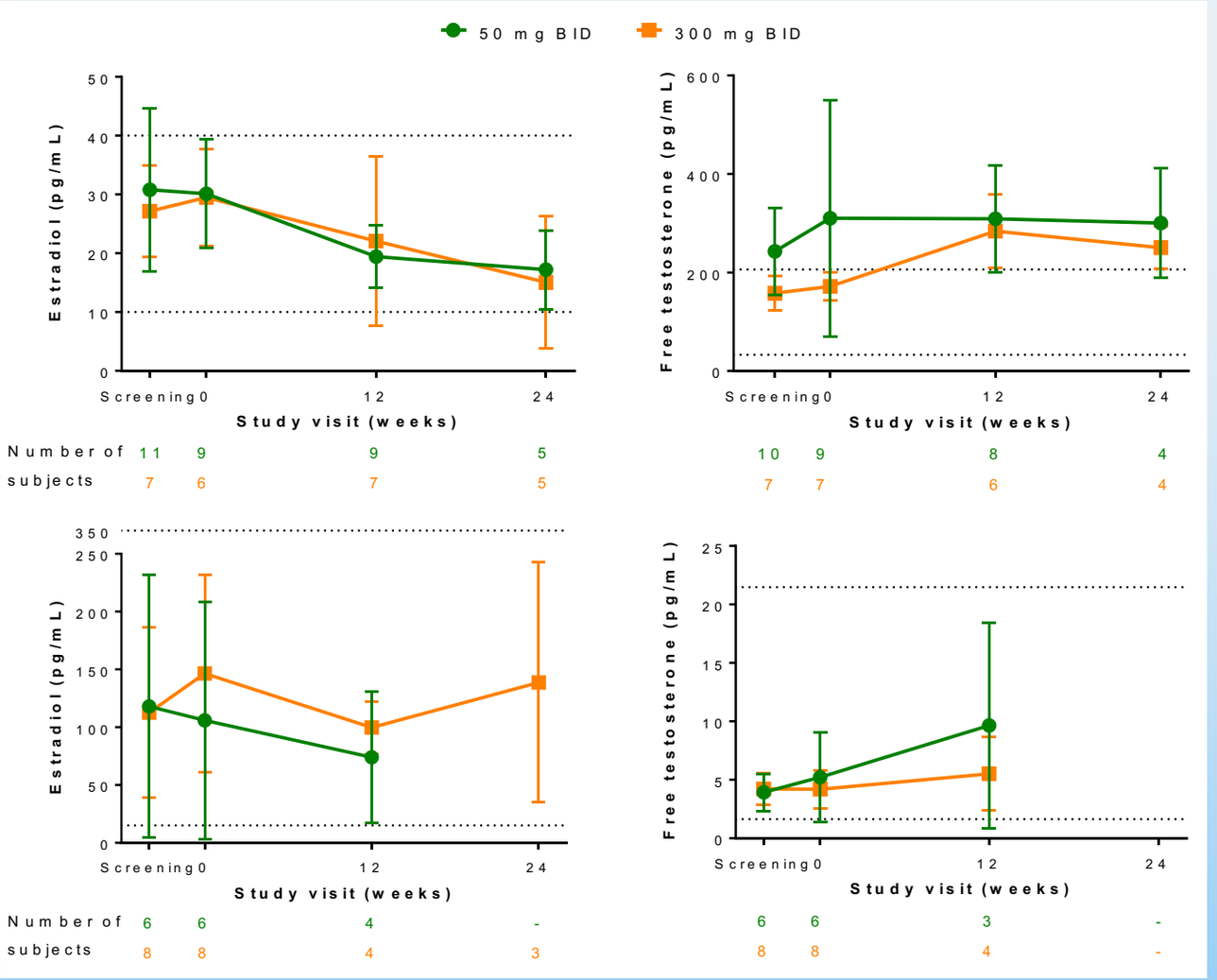
Effect of AG-348 on Hormones

Preliminary findings are consistent with aromatase inhibition by AG-348

Male

- Hormone levels assessed at baseline, 12 and 24 weeks
- Patients with available data shown

Female



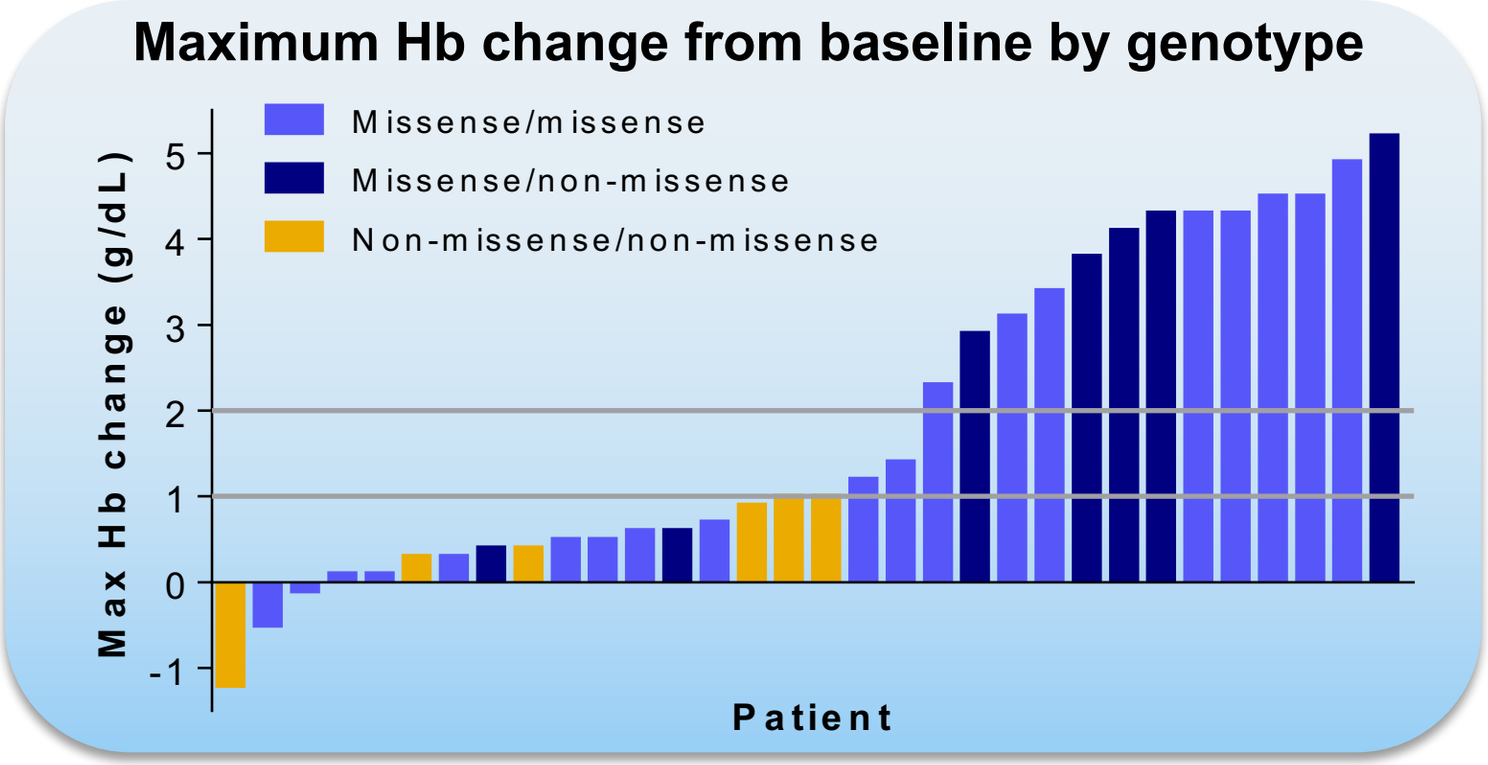
22 Data presented at ASH 2016, 12/4

Normal reference low and high limits shown as horizontal dotted lines

Clinical Activity Results

Maximum Increase in Hemoglobin (Hb)

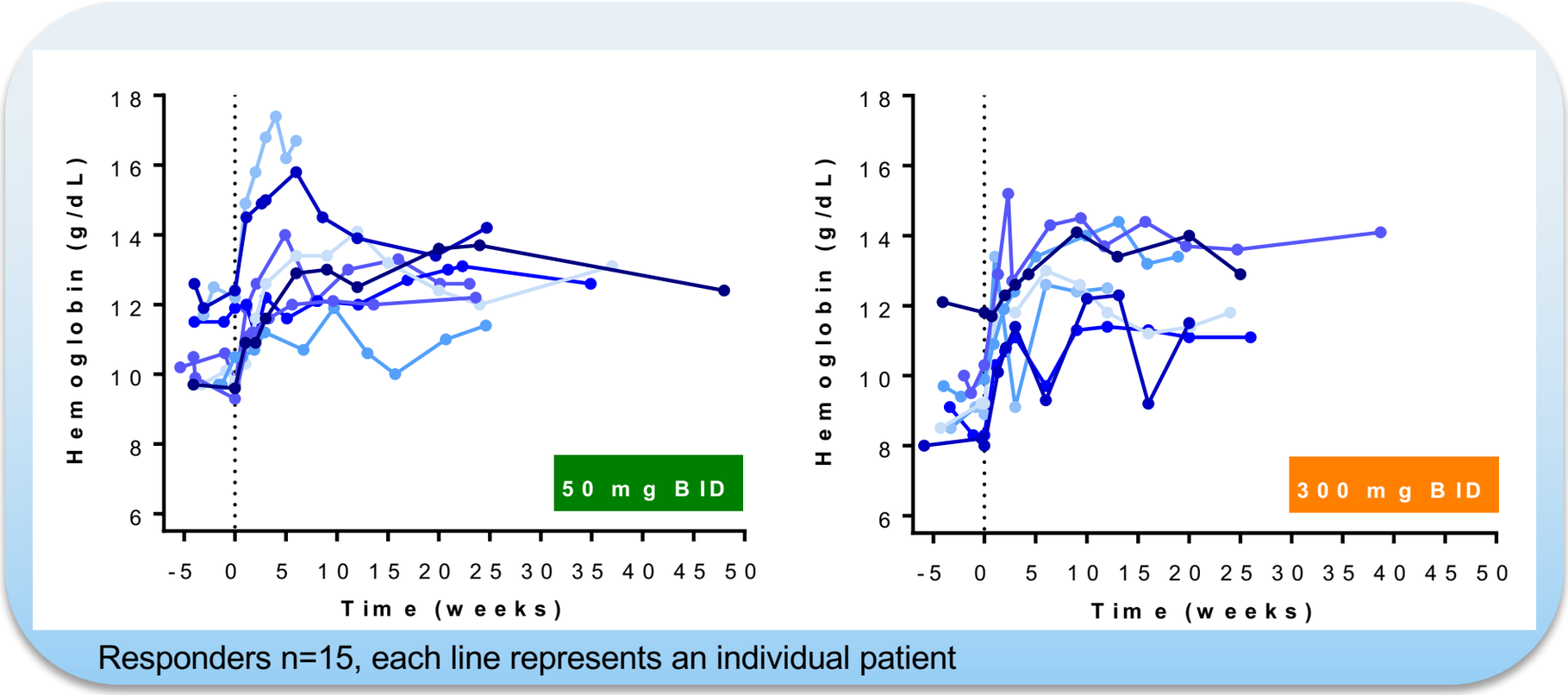
- 15 of 32 (47%) patients had a maximal increase in Hb >1.0 g/dL
  - 15 of 26 patients (58%) who had ≥1 missense mutation had a Hb response
- 5 patients homozygous for R479H (mis/mis; Amish) were non-responders
- Hb response and response maintenance are seen across a range of 4 doses
  - Robust Hb responses led to dose decreases with maintained Hb



 Data presented at ASH 2016, 12/4

Hb Increases Are Rapid and Sustained

- In patients who had Hb increases >1.0 g/dL (n=15):
  - Median time to Hb increase >1.0 g/dL was 1.4 weeks (range, 1.1–21.0)
  - The mean maximum increase was 3.6 g/dL (range, 1.2–5.2)
- 10 patients had dose reductions: 5 due to rapid Hb increase[a]

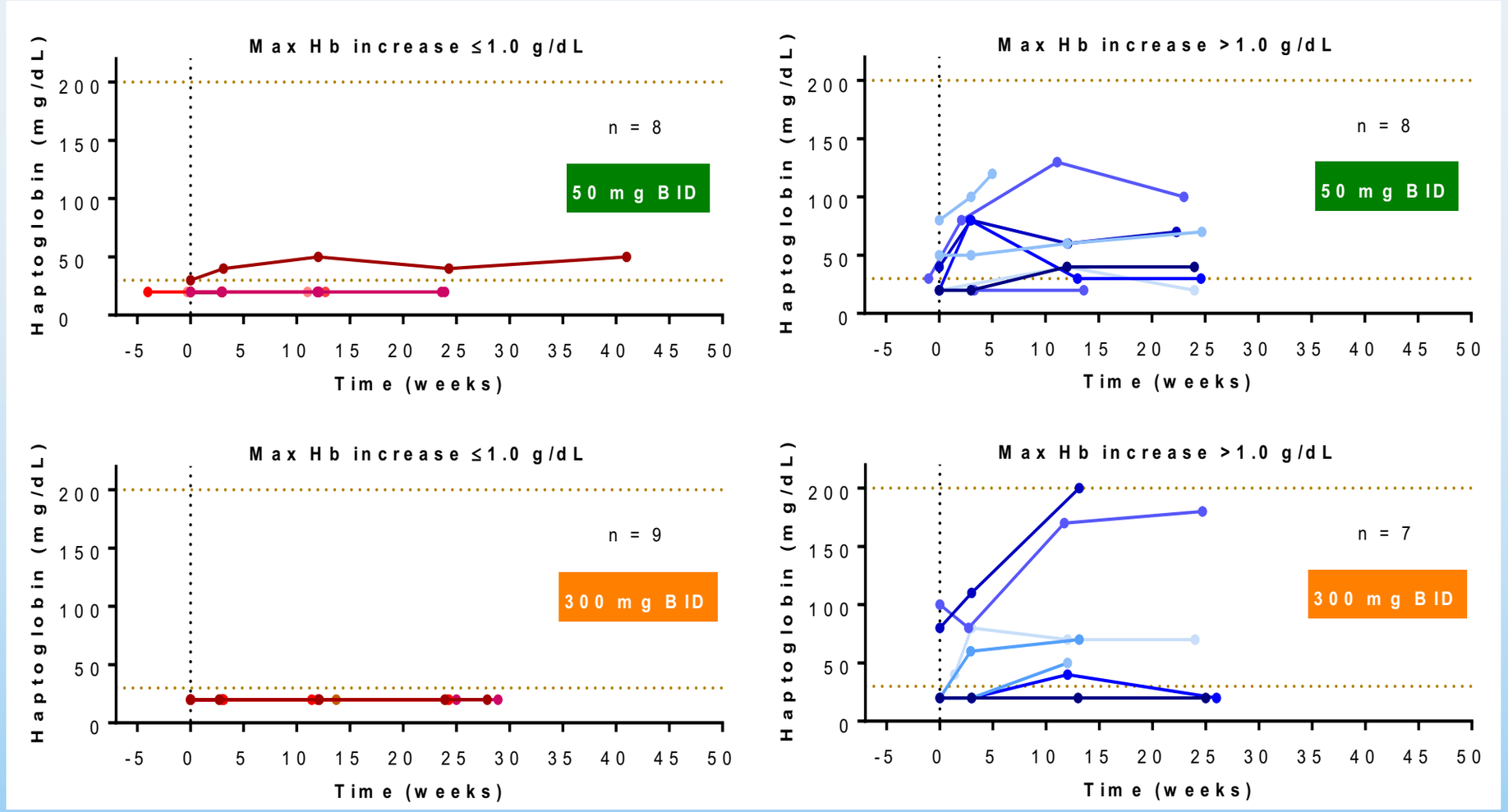


Responders n=15, each line represents an individual patient

[a]Other dose reductions due to: AEs (n=3), self-reduction due to fatigue (n=1), taper prior to discontinuation (n=1)

Data presented at ASH 2016, 12/4

Haptoglobin Levels Increase in Responders, Indicating Decreased Hemolysis



 Data presented at ASH 2016, 12/4

Normal reference low and high limits shown as horizontal dotted lines

DRIVE PK Conclusions

- AG-348 is a novel, first-in-class, PK-R activator in clinical testing as a potential disease-altering therapy to improve anemia in patients with PK deficiency
- Daily dosing with AG-348 for up to 6 months is well tolerated
  - Clinical significance of AG-348 aromatase inhibition remains unclear
- AG-348 demonstrates clinically relevant rapid and durable increases in Hb in 47% of patients enrolled in the study
  - Hb increase is linked to activation of glycolytic pathway
  - Preliminary genotype-Hb response correlations were observed
- These data highlight the potential of PK-R activators as the first disease-altering treatment for patients with PK deficiency

 Data presented at ASH 2016, 12/4

AG-519 Phase 1 Data Overview

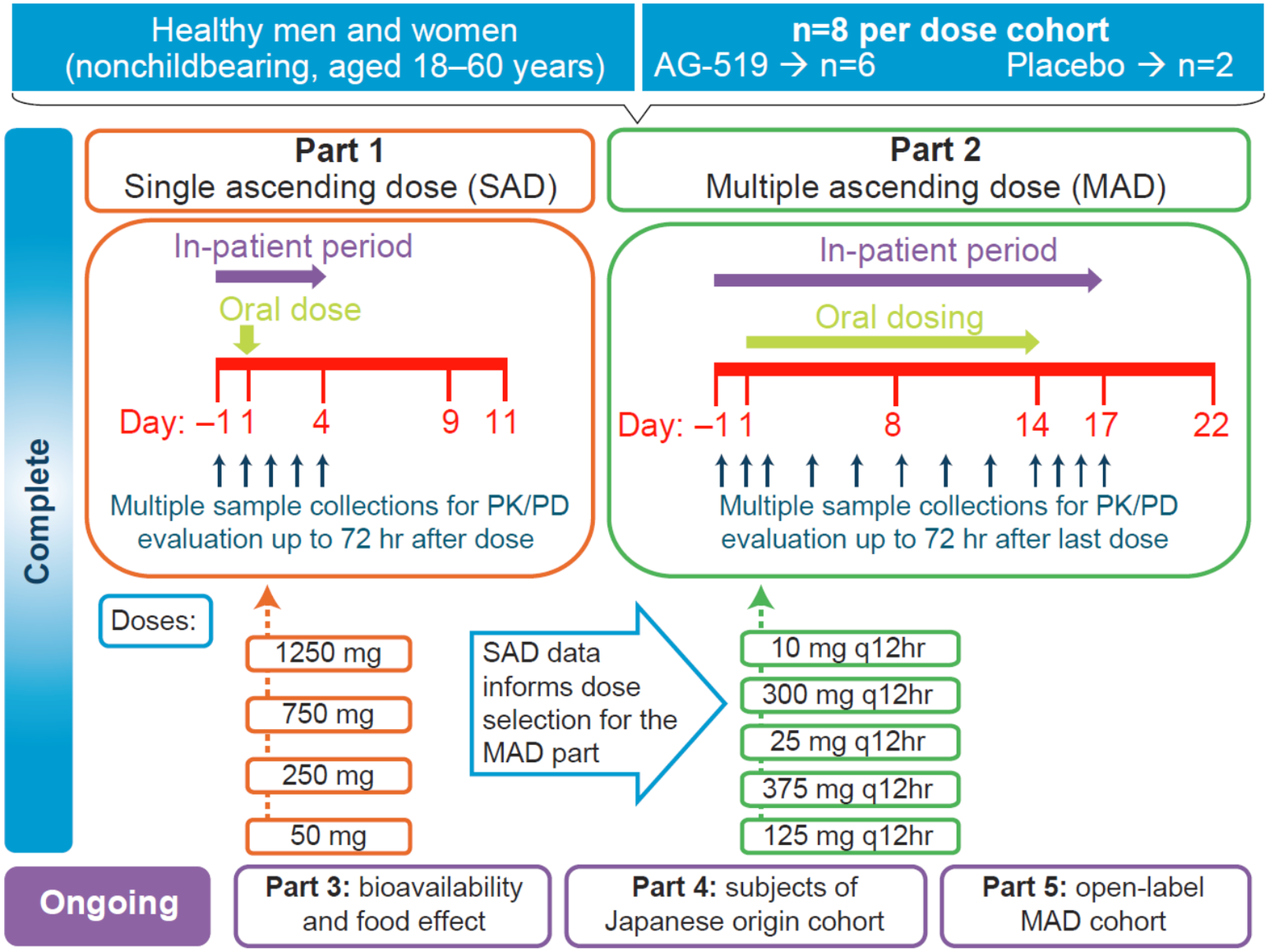
Chris Bowden, M.D.
Chief Medical Officer

AG-519 Is a Second PKR Activator in Clinical Development

- Potent, selective and orally bioavailable
- Comparable biochemical, cellular and in vivo activity to AG-348
- No aromatase inhibition
- Ongoing Phase 1 study in healthy volunteers
  - Identify a safe and pharmacodynamically active dose and schedule

 Data presented at ASH 2016, 12/3

AG-519 Phase 1 Study Design and Status



 Data presented at ASH 2016, 12/3

AG-519 Demographic and Baseline Characteristics

Characteristic	SAD		MAD	
	Placebo n=8	Pooled AG-519 n=24	Placebo n=10	Pooled AG-519 n=30
Men, n (%)	7 (87.5)	20 (83.3)	7 (70)	28 (93.3)
Age in years, mean (range)	37.8 (18–58)	41.5 (19–58)	42.8 (18–57)	38.4 (19–59)
Body mass index kg/m^2, mean (range)	24.8 (21.9–27.4)	26.8 (19.3–31.1)	27.7 (24.8–30.9)	26.2 (20.6–31.3)
Race, n (%)				
White	8 (100)	21 (87.5)	9 (90)	27 (90)
Black	0	3 (12.5)	0	1 (3.3)
Asian	0	0	1 (10)	0
Other	0	0	0	2 (6.7)
Ethnicity, n (%)				
Not Hispanic or Latino	8 (100)	24 (100)	10 (100)	30 (100)

 Data presented at ASH 2016, 12/3

AG-519 Safety Summary

- All AEs were mild or moderate (Grade 1 or 2); headache most common
- As previously reported, a single case of Grade 2 thrombocytopenia in a subject receiving 375 mg AG-519 q12hr, which resolved spontaneously within 7 days after the last dose
- One ongoing SAE of drug-related cholestatic hepatitis was reported* (bioavailability and food effect study; 300 mg); this event is being further evaluated

*Reported after data cutoff

Data presented at ASH 2016, 12/3

AG-519 Summary of Adverse Events

AEs	SAD		MAD	
	Placebo n=8	Pooled AG-519 n=24	Placebo n=10	Pooled AG-519 n=30
Subjects experiencing any AE, n (%)	2 (25)	8 (33.3)	5 (50)	17 (56.7)
Grade 1–2	2 (25)	8 (33.3)	5 (50)	17 (56.7)
Grade ≥3	0	0	0	0
Subjects experiencing any SAE, n (%)	0	0	0	0
Subjects experiencing any AE leading to discontinuation, n (%)	0	0	0	0
Most common AEs (≥2 subjects in pooled AG-519 group), n (%)				
Headache	1 (12.5)	3 (12.5)	2 (20)	9 (30)
Nasopharyngitis	0	3 (12.5)	0	2 (6.7)
Diarrhea	0	1 (4.2)	0	2 (6.7)
Rash	0	0	0	2 (6.7)
Subjects experiencing any treatment-related AE, n (%)[a]	0	2 (8.3)	0	4 (13.3)
Treatment-related AEs occurring in ≥2 subjects	0	0	0	0

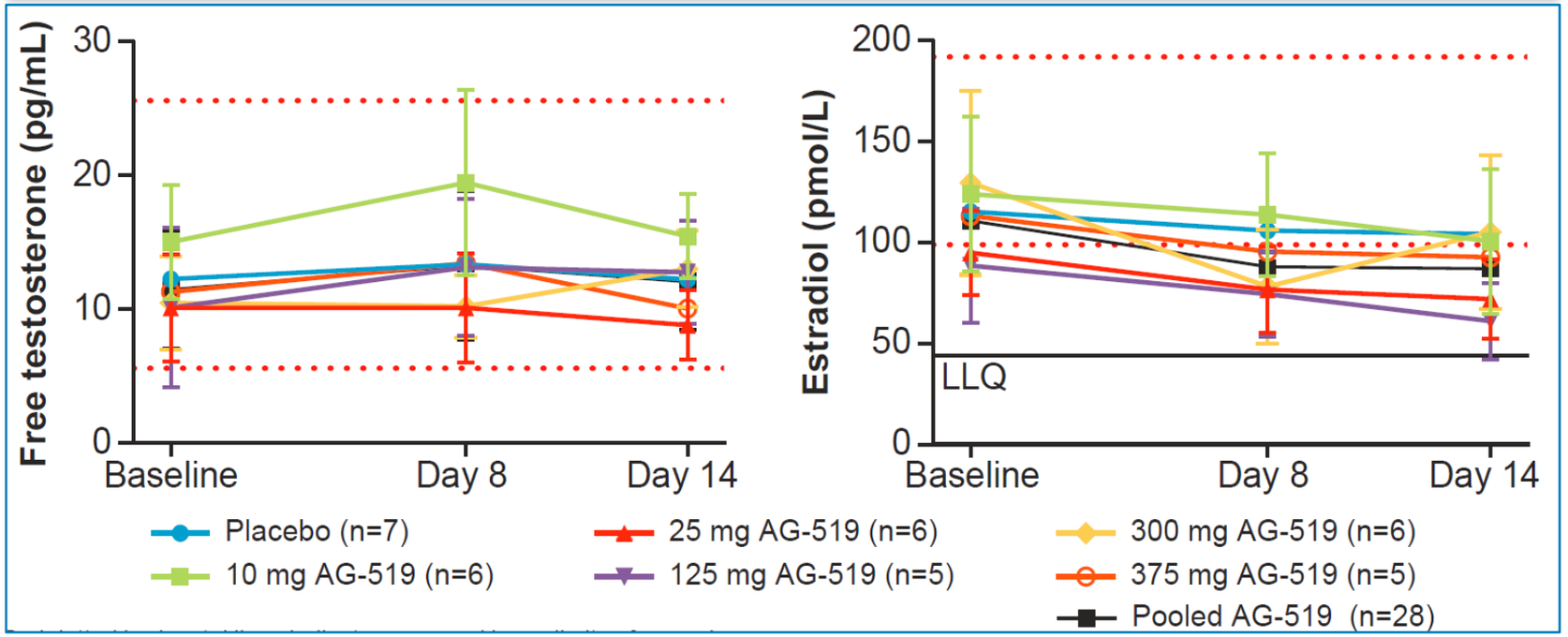
[a]Judged possibly or probably related to treatment

 Data presented at ASH 2016, 12/3

AG-519 Shows No Effects on Sex Steroids in Healthy Volunteers

Analysis of free testosterone and estradiol indicated the absence of aromatase-inhibitory activity, as expected

Free testosterone and serum estradiol in male subjects in MAD study

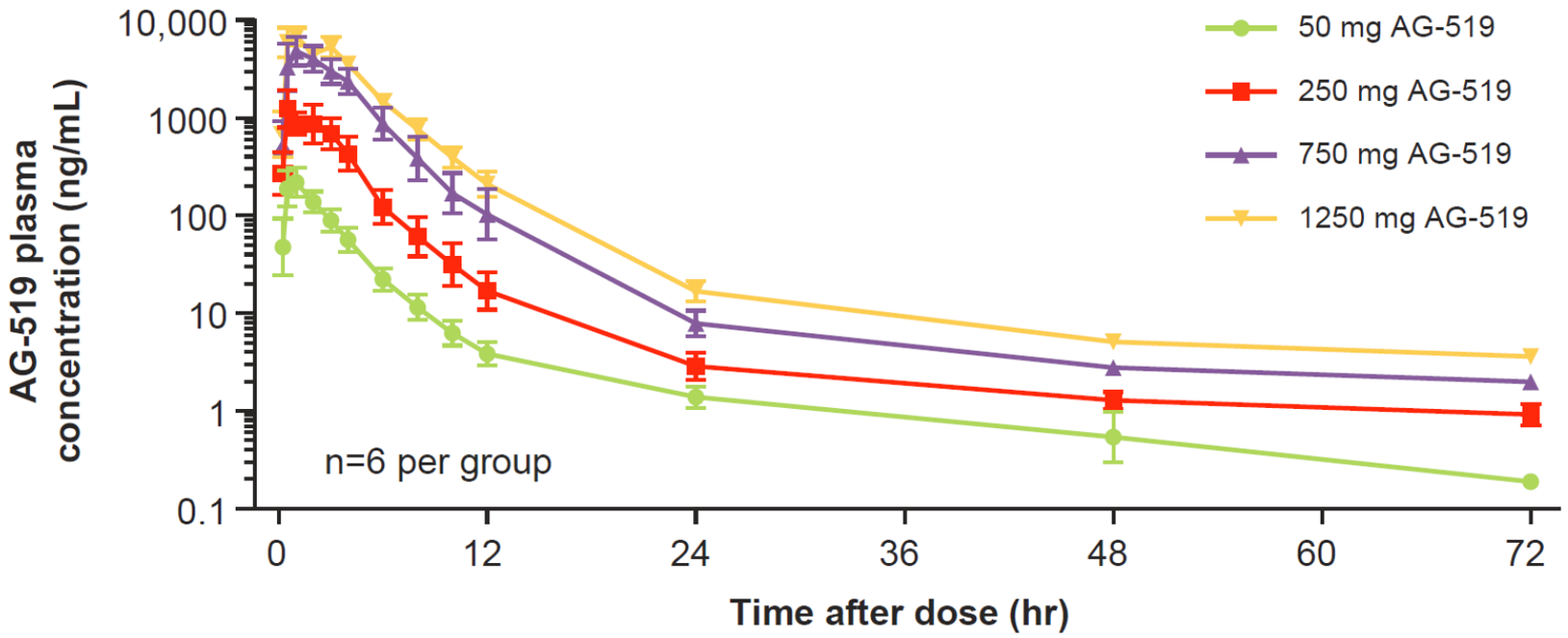


 Data presented at ASH 2016, 12/3

AG-519 Pharmacokinetics (PK) Profile Supports Twice Daily Dosing

- Rapid absorption, moderate variability
- Exposure is approximately dose-proportional
- Effective half-life of approximately 6 hours
- Similar PK profile observed in MAD portion

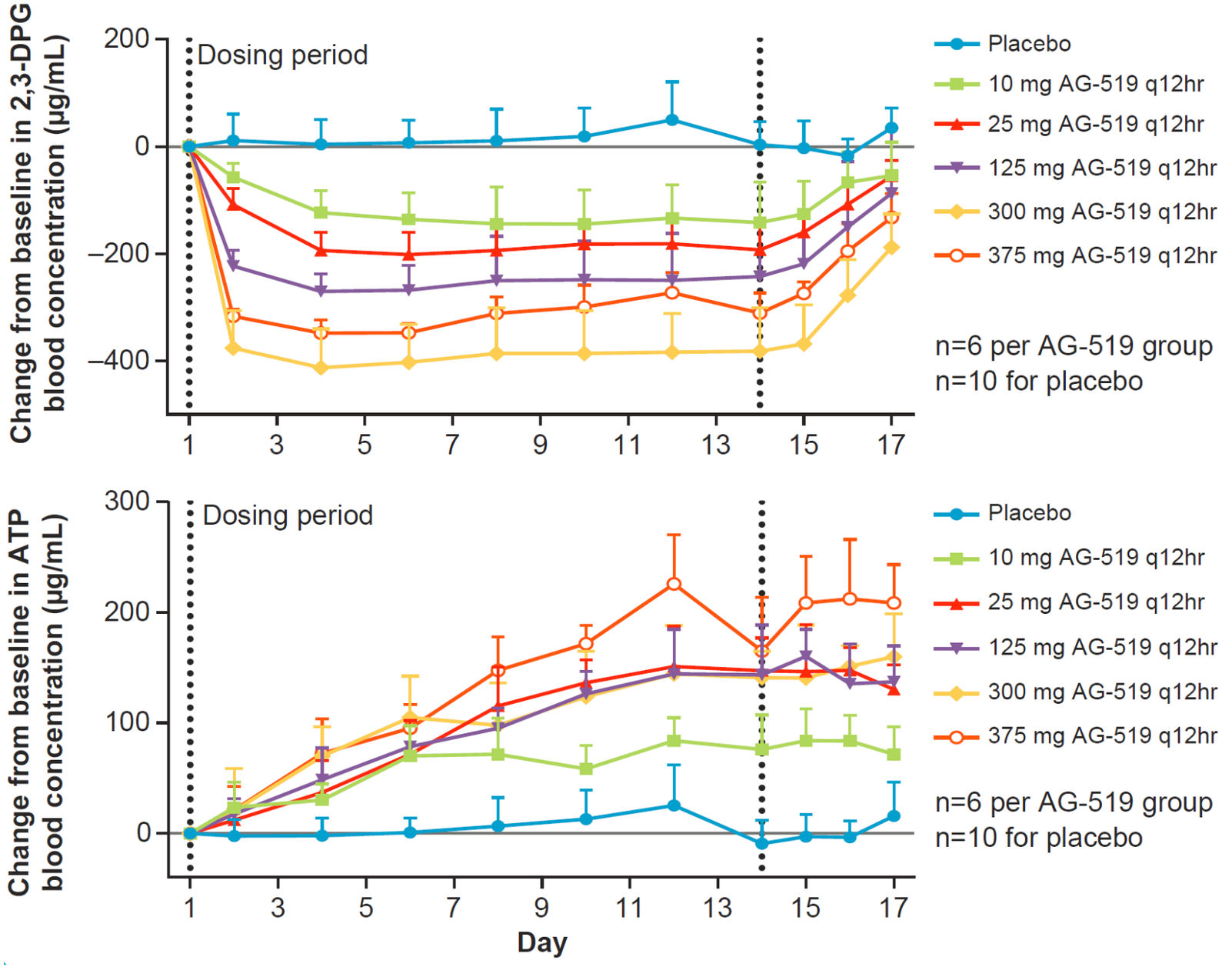
Mean (SD) plasma concentration-time profiles of AG-519 following a single oral dose



 Data presented at ASH 2016, 12/3

AG-519 Demonstrates Robust Pharmacodynamics Effects

- Mean decrease of 61% in blood 2,3-DPG levels
- Mean increase of up to 63% in blood ATP levels, peaking at Day 12
- Profile comparable to AG-348



 Data presented at ASH 2016, 12/3

AG-519 Conclusions

- Well-tolerated, up to 14 days of twice daily dosing in healthy volunteers
- Favorable pharmacokinetic profile
- Robust dose-dependent changes in ATP and 2,3-DPG blood levels consistent with increased PKR activity
- Data demonstrate activity of AG-519 as an PKR activator is comparable to that of AG-348

 Data presented at ASH 2016, 12/3

PKR Program Moving Toward Pivotal Development

Pivotal Dose for Either Molecule Likely Less Than or Equal to 50 mg

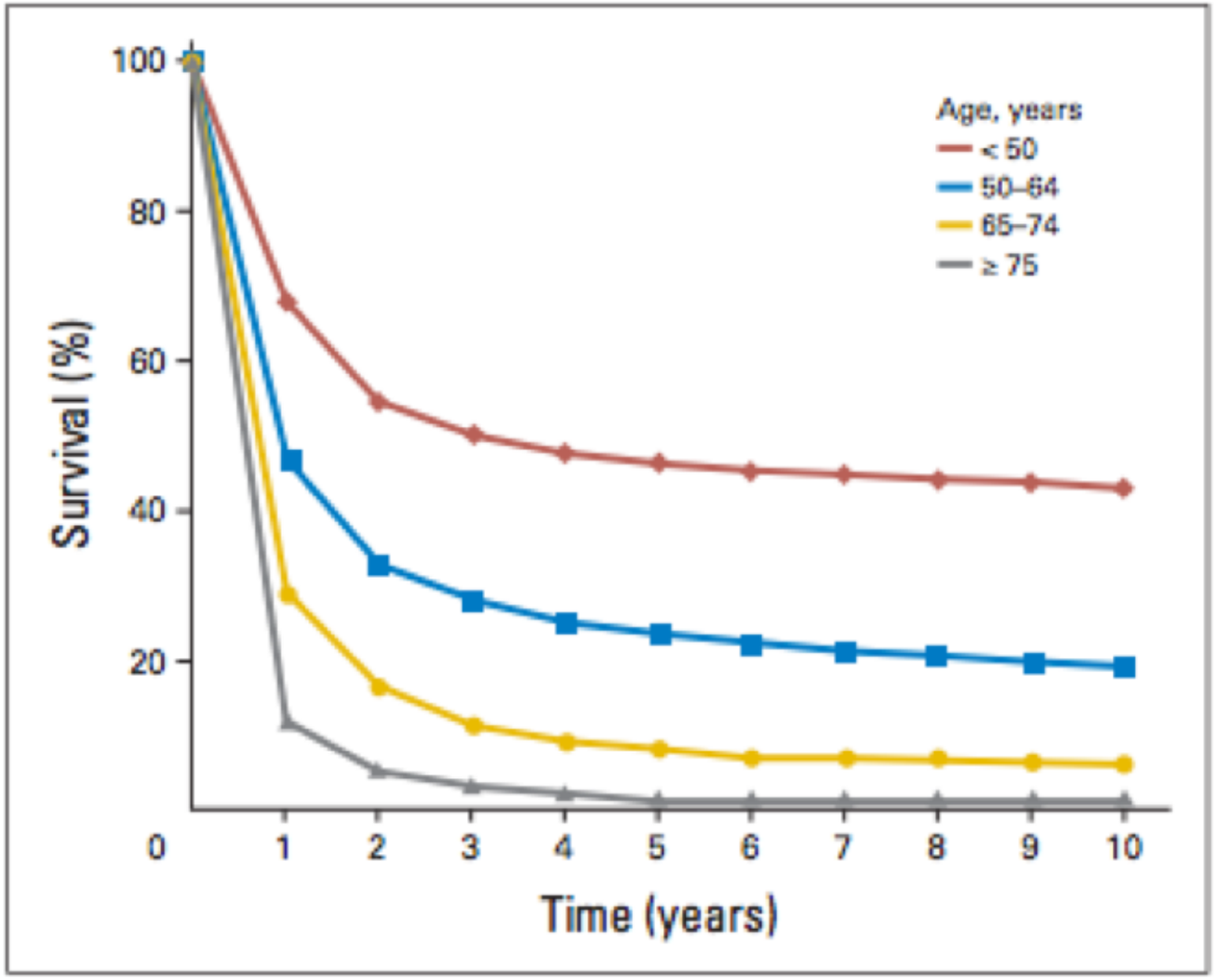
IDHm Inhibitors & AML Landscape

Eytan Stein, M.D.
Memorial Sloan-Kettering Cancer Center

AML Is a Devastating Blood Cancer

- Most common leukemia in adults
- Rapid growth of abnormal white blood cells interfere with normal blood cell production
- Few treatment options, with no improvements in decades
- 5-year survival rate is 20-25%
- Median age at diagnosis 68-72 years
- Many cannot tolerate standard of care chemotherapy or transplant

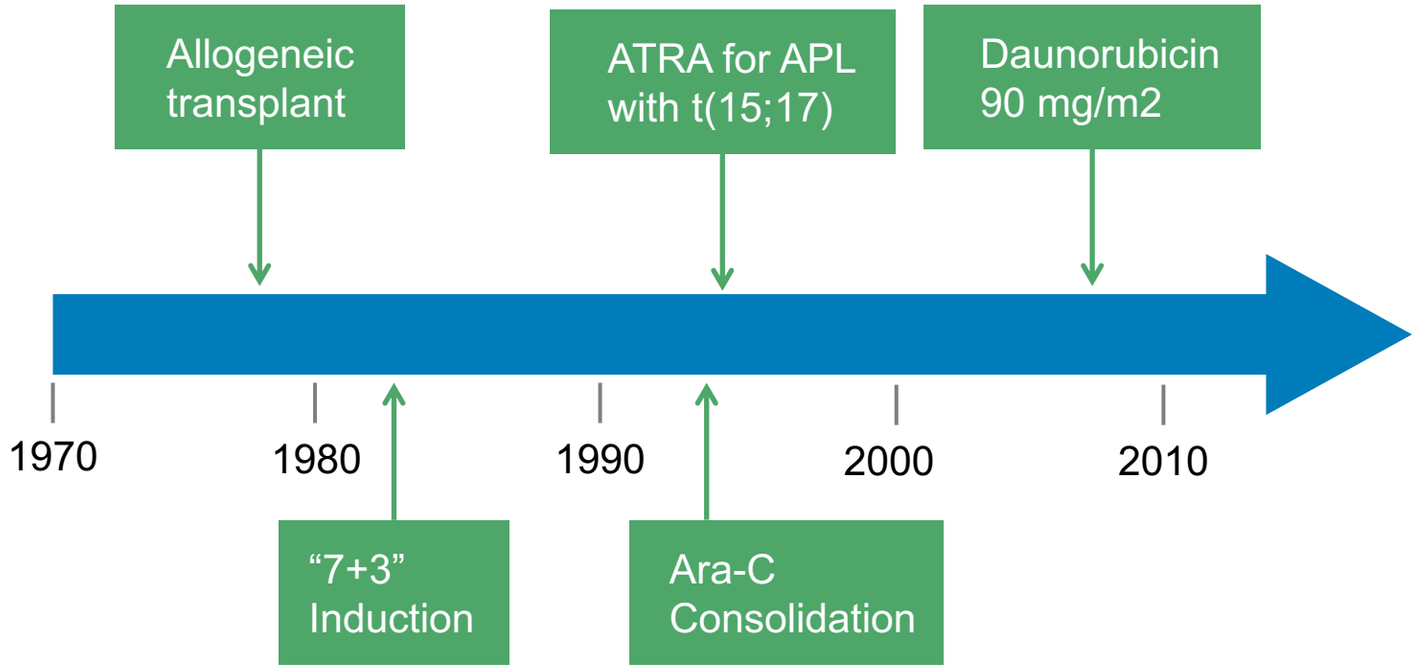
Relative survival by time & age of AML based on SEER



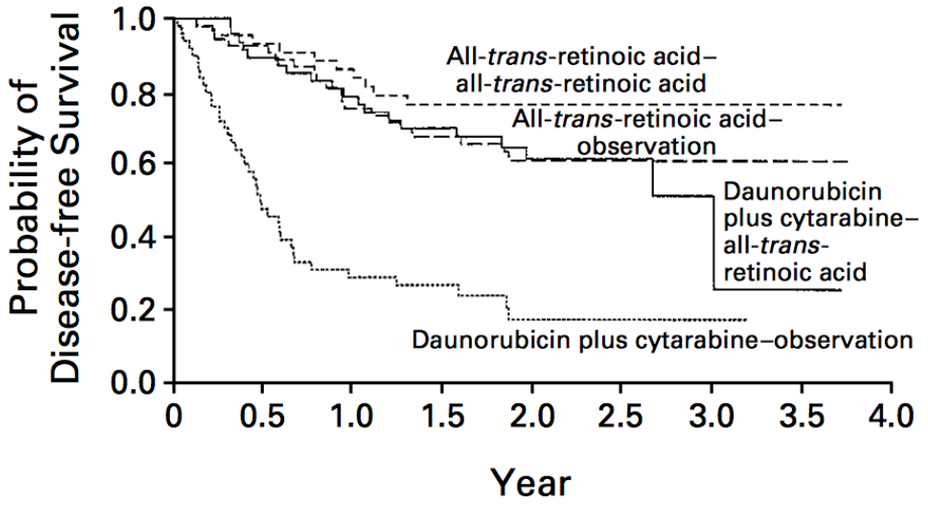
Klepin, et al, JCO, 32, 2014

Siegel R, et. al. CA Cancer J Clin. 2012 Jan-Feb;62(1):10-29.

Few Advances in AML in Decades



Acute Promyelocytic Leukemia (APL)

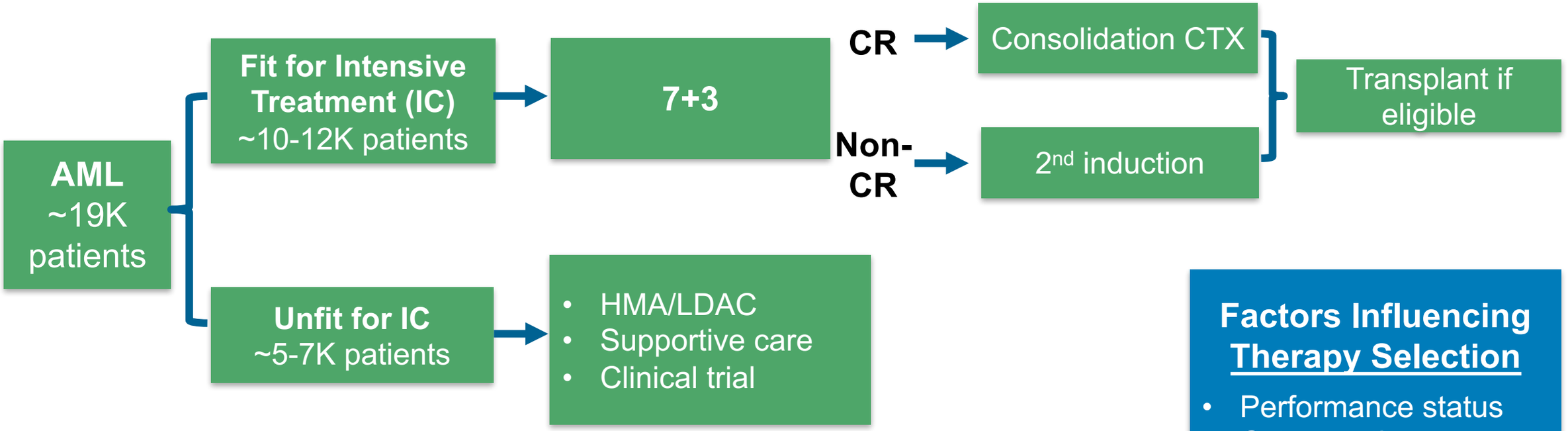


All-trans retinoic acid (ATRA) induces terminal differentiation of APL cells, leading to cures when combined with other therapies

Thomas ED, N Engl J Med. 1979 Mayer, N Engl J Med. 1994, Fernandez H,N Engl J Med, 2009

Tallman M, N Engl J Med. 1997.

Treatment Options for Newly Diagnosed AML



Factors Influencing Therapy Selection

- Performance status
- Cytogenetics
- Molecular analysis

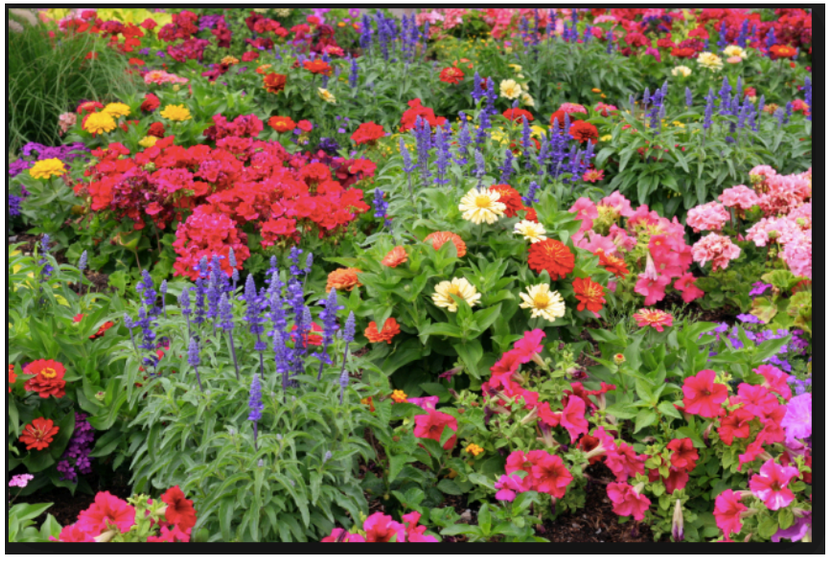
CTX = Chemotherapy
HMA = Hypomethylating Agent
LDAC = Low dose Cytarabine

Thol F, Blood. 2015.

First in Class IDHm Inhibitors Are Transforming the Treatment of AML

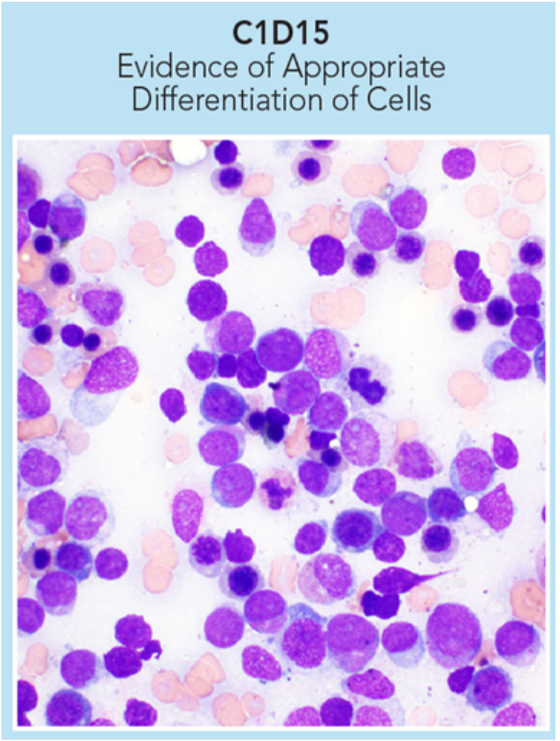
Chemotherapy

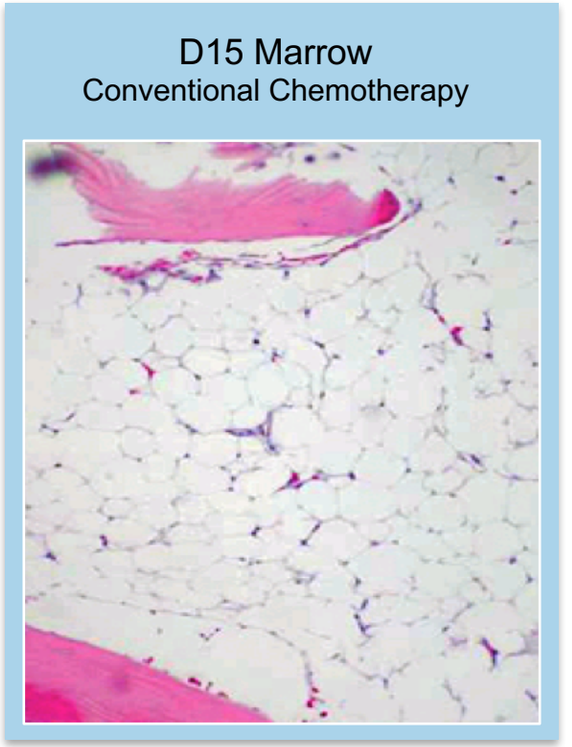
IDHm Inhibitors



IDHm Inhibitor Response Fundamentally Different from Chemotherapy

Maturation of mutated cells in response to IDHm treatment through the first cycle





Biopsy post conventional chemotherapy shows an empty marrow

Acute Myeloid Leukemia (AML)				
Incidence (cases/year U.S.)	Prevalence (U.S.)	IDH1m frequency	IDH2m frequency	5-year overall survival
~19K	~25K	6-10%	9-13%	20-25%

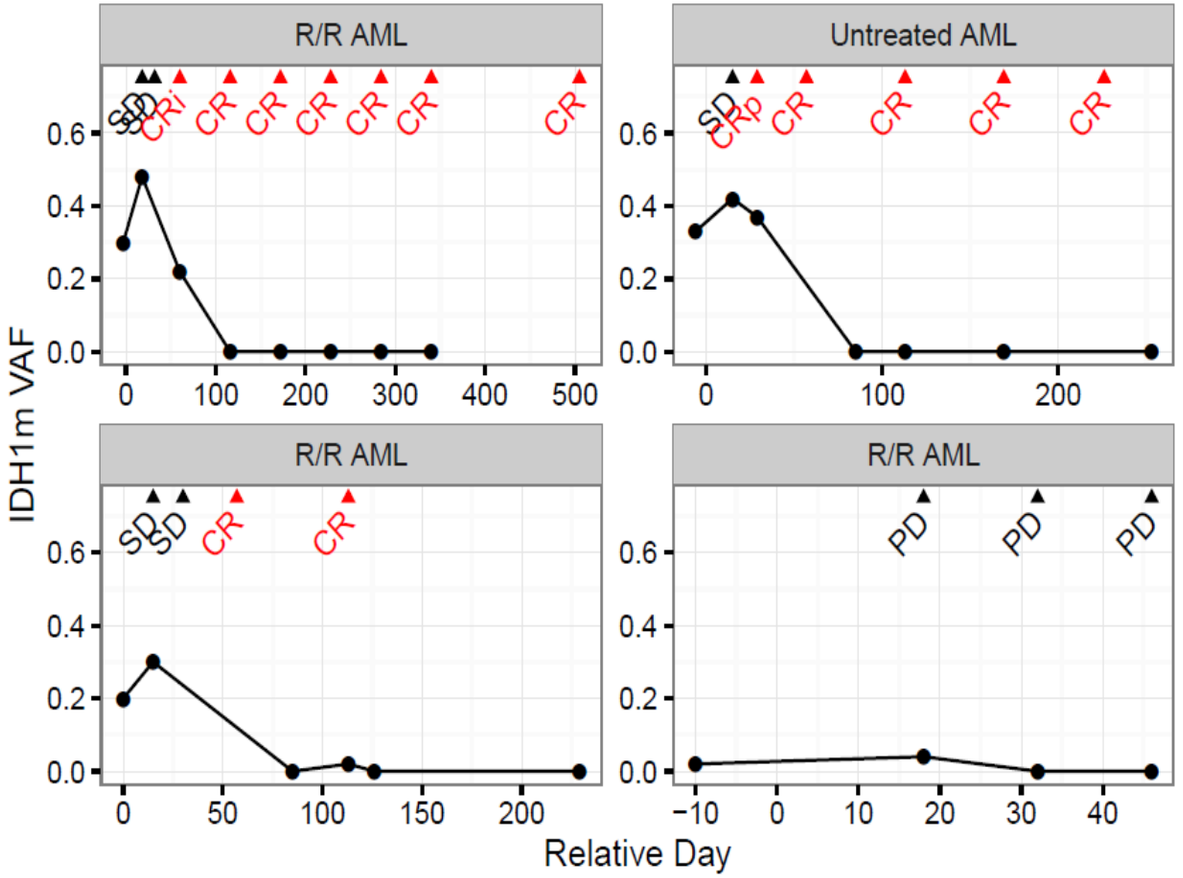
Image: Min Xu M.D.
Data Presented at AACR, 4/2014
Multiple sources including market research SEER

First Demonstration that Treatment with AG-120 Alters Underlying Biology of AML

- Updated data from 78 patients in Phase 1 dose escalation:
  - 38% ORR (30/78), 18% CR (14/78)
- Longitudinal mIDH1 variant allele frequency (VAF) data for 51 patients
- First demonstration single agent AG-120 treatment can result in mIDH1 clearance

Data to be updated Monday 12/5/16 at 4:45pm PT
Marriott Marquis San Diego, Ballroom AB
Session Title: 616. Acute Myeloid Leukemia: Novel Therapy, excluding Transplantation: FLT3 and IDH Targeted Therapies in AML

VAF Analysis Using FoundationOne® Heme NGS Assay Demonstrates mIDH1-MC in 4 AML Patients Treated with AG-120



ORR = overall response rate; CR=complete remission

DiNardo, C, et.al. ASH 2016. Abstract 1070

Closing Remarks

David Schenkein, M.D.
Chief Executive Officer

Key Takeaways

PKR

- Updated DRIVE PK data continue to demonstrate clinically meaningful impact on hemoglobin with additional patients and longer follow-up
- Clear proof-of-mechanism for AG-519, with activity as a PKR activator comparable to that of AG-348
- Program heading into pivotal development

IDH

- Executing late-stage clinical development for enasidenib and AG-120
- Updated Phase 1 dose escalation data in abstract confirm AG-120's robust, durable clinical activity as a single agent
- First demonstration that AG-120 changes the biology of disease through mutational clearance of IDH1