Agios: Delivering Our First Medicines to Patients

JPMorgan Healthcare Conference

January 9, 2017

David Schenkein, M.D.
Chief Executive Officer

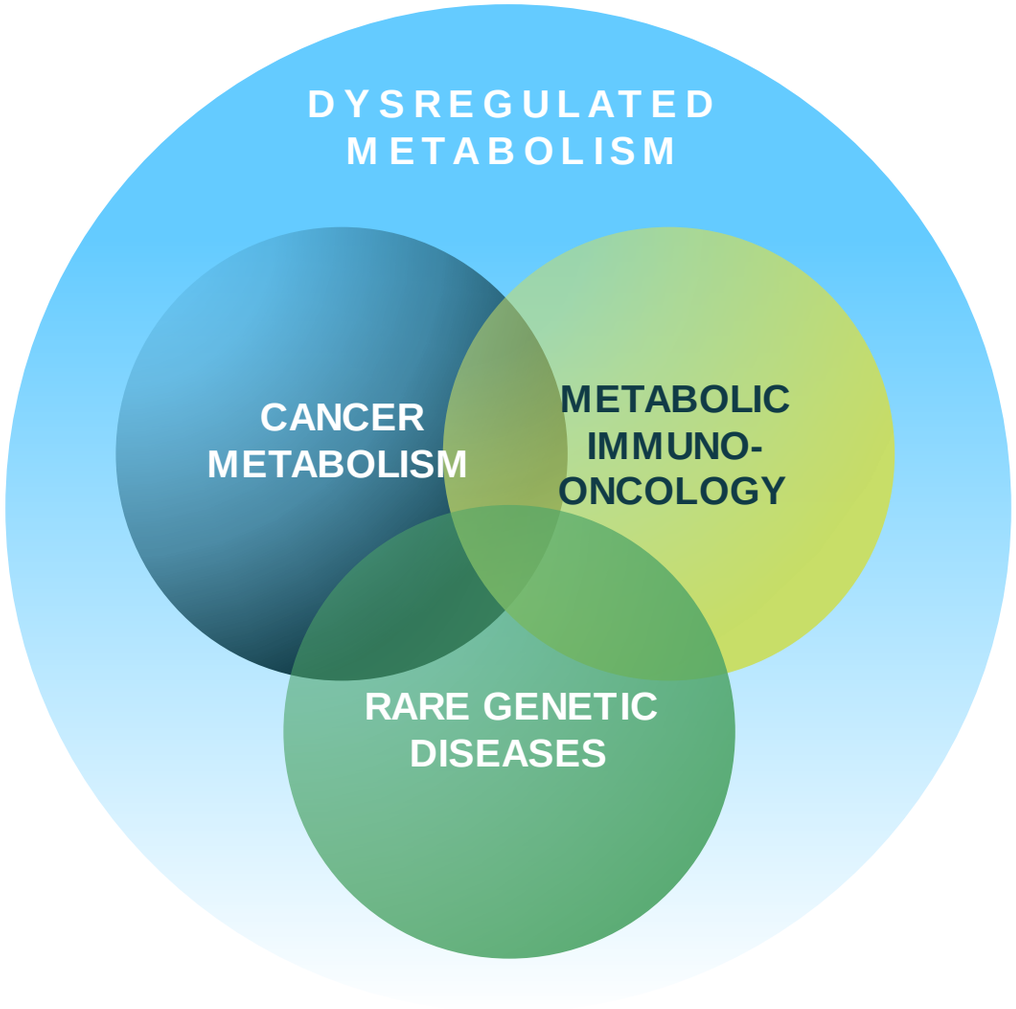
Forward Looking Statements

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 the Agios' plans, strategies and expectations for its and its collaborator's preclinical, clinical and commercial advancement of its drug development programs including enasidenib, AG-120, and AG-348; the potential benefits of Agios' product candidates; its key milestones for 2017; its financial guidance regarding the period in which it will have capital available to fund its operations; 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," "strategy," "milestone," "will," 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 collaborator, Celgene, 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: 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' Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, and other filings that Agios may make with the Securities and Exchange Commission in the future. 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.

How a Clinical Trial Gave Me My Life Back After MDS and AML

BY SHIRLEY O'BRIEN
Oct. 2016

We Are Driven By a Clear Vision and Values



agios

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 diseases.

Building a Global, Commercial-Stage Biopharmaceutical Company

January 2009

2009

January 9, 2017

Delivering Our First Medicines to Patients

2017 Key Priorities & Expected Milestones

IDH

- Secure approval and co-commercialize enasidenib for R/R AML in the U.S.
- Submit NDA for wholly owned AG-120 in R/R AML by YE 2017
- Initiate Phase 3 combining AG-120 and VIDAZA® in frontline AML in 1H 2017

PKR

- Continue to demonstrate leadership in PK deficiency
- Prepare for 1H 2018 pivotal trial initiation for wholly owned AG-348 in PK deficiency

RESEARCH

- Advance next wave of research in three areas of expertise: cancer metabolism, rare genetic diseases and metabolic immuno-oncology
- File IND application for MTAP pathway development candidate by YE 2017

2017 – 2018

Commercial Stage Biopharmaceutical Company

2	4+	3+	3	450+	100%
approved precision medicines in AML	clinical-stage molecules	pivotal trials (IDH, PKR)	areas of research expertise	employees	committed to helping patients

Delivering Our First Medicines to Patients

Team

Science

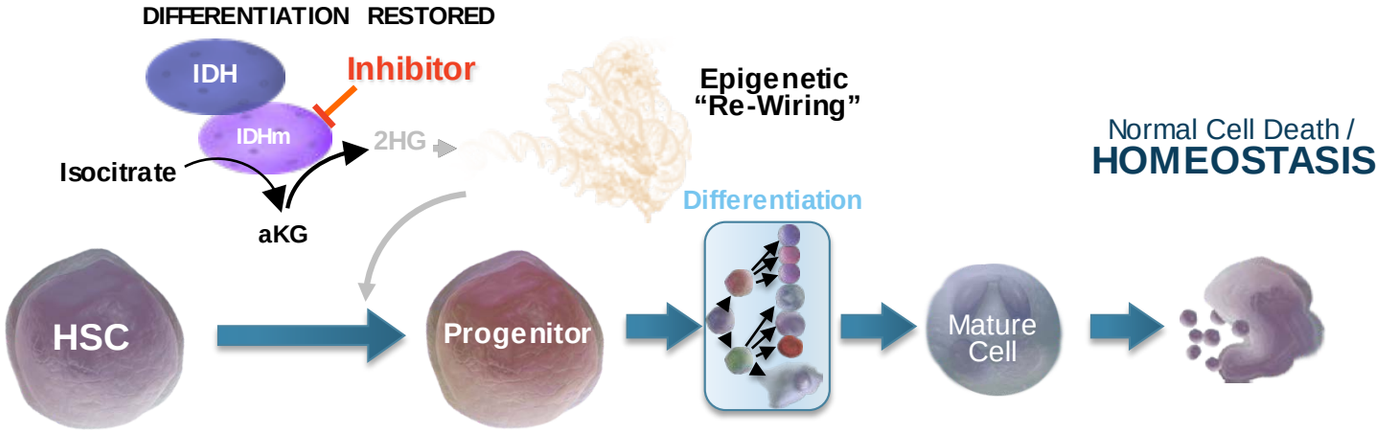
Discovery

IDH

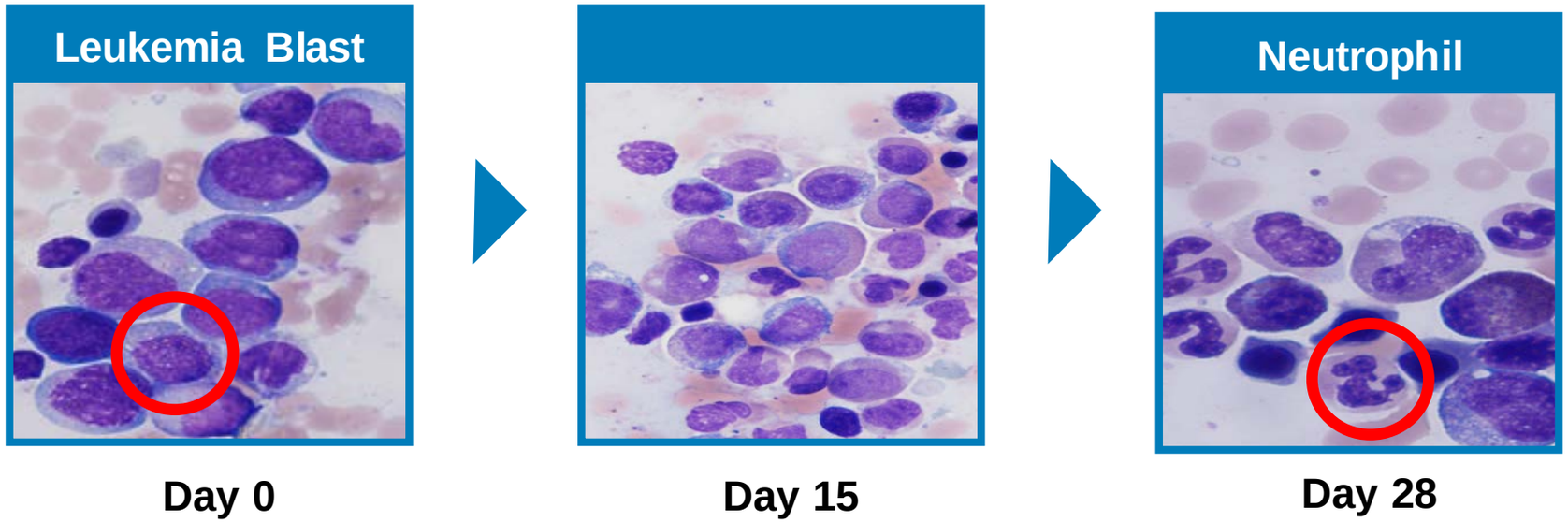
PKR

RESEARCH

Repairing an IDH Mutant Cancer Cell



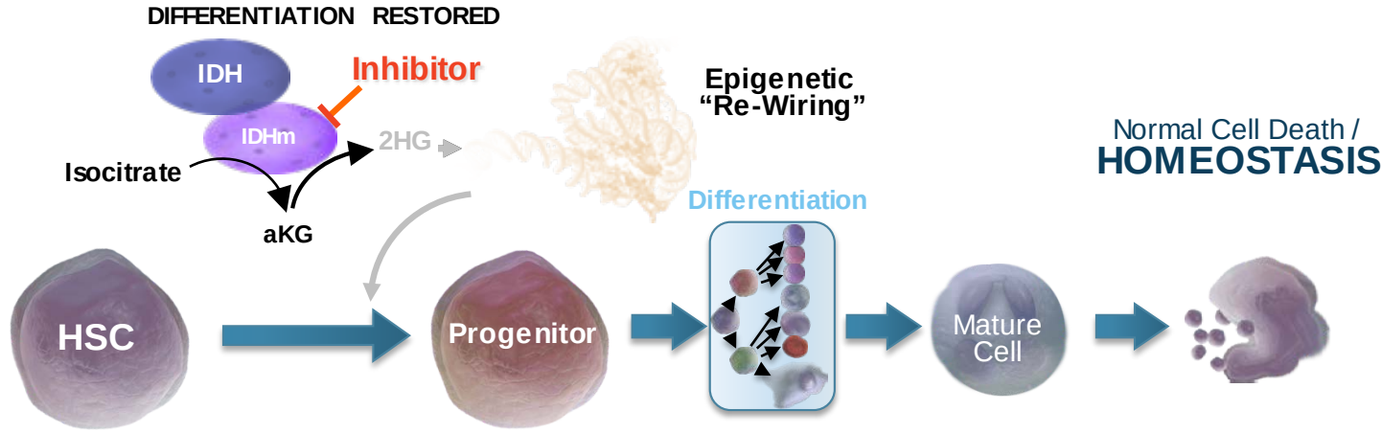
IDHm Inhibitor

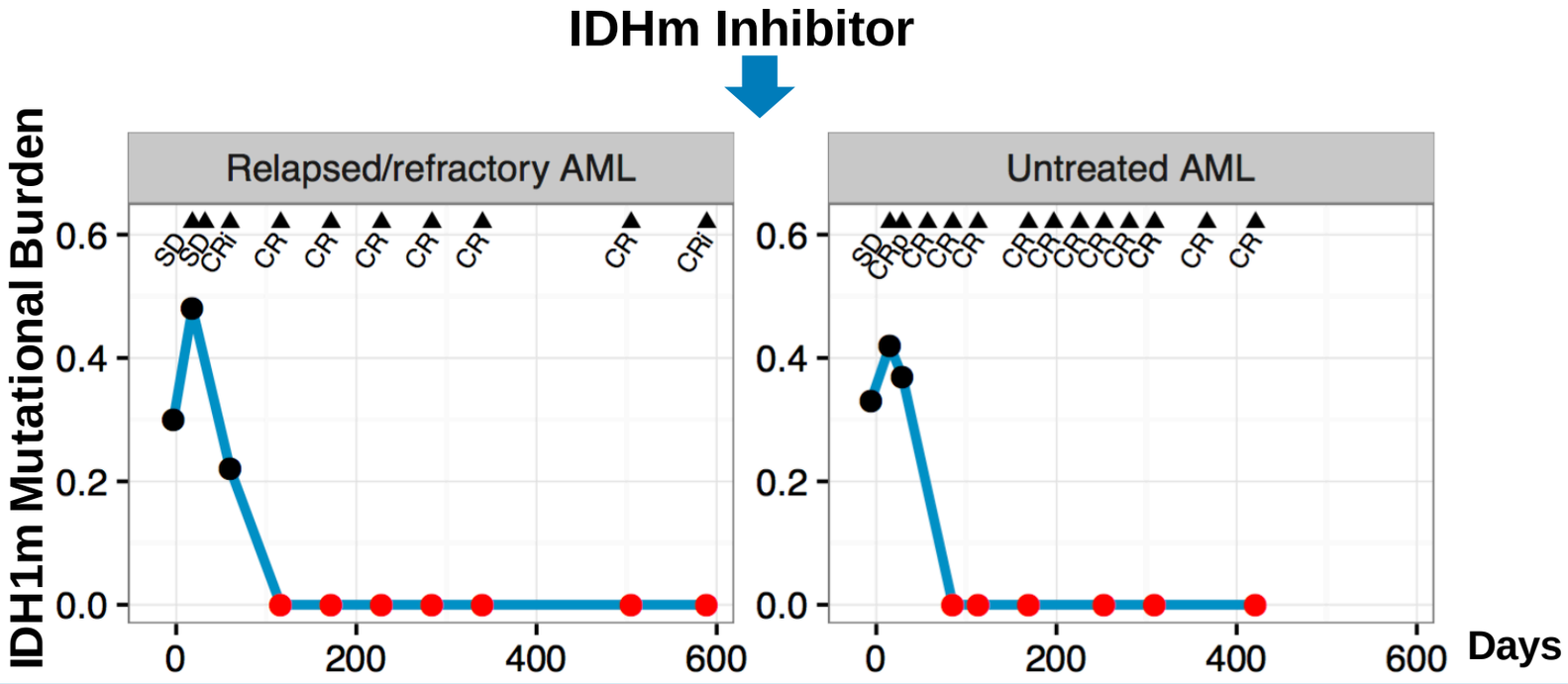


AG-120, EORTC, 2014

Mutation occurs early and persists throughout illness

Repairing an IDH Mutant Cancer Cell





Mutation occurs early and persists throughout illness

AG-120, ASH, 2016

Our Vision for IDHm Inhibitors

A Roadmap for Speed and Breadth

All IDHm patients screened and treated with an IDHm inhibitor for the entire course of their disease

Our Vision for IDHm Inhibitors

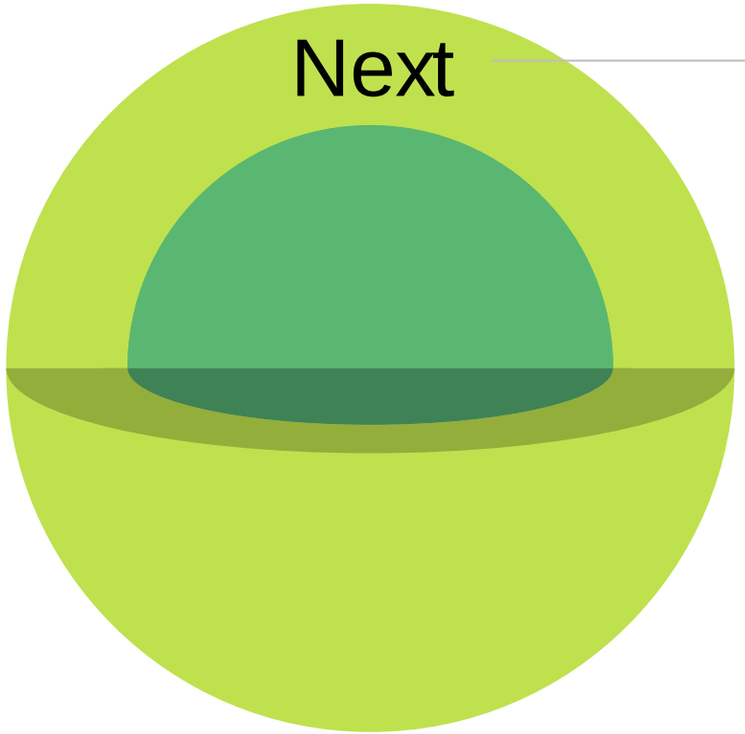
A Roadmap for Speed and Breadth

Relapsed/Refractory AML

- ✓ Enasidenib NDA submission 2016
- ▪ AG-120 NDA submission by YE 2017

Our Vision for IDHm Inhibitors

A Roadmap for Speed and Breadth



Frontline AML

- AG-120 + Vidaza® Phase 3
- Enasidenib / AG-120 + (7+3) with maintenance

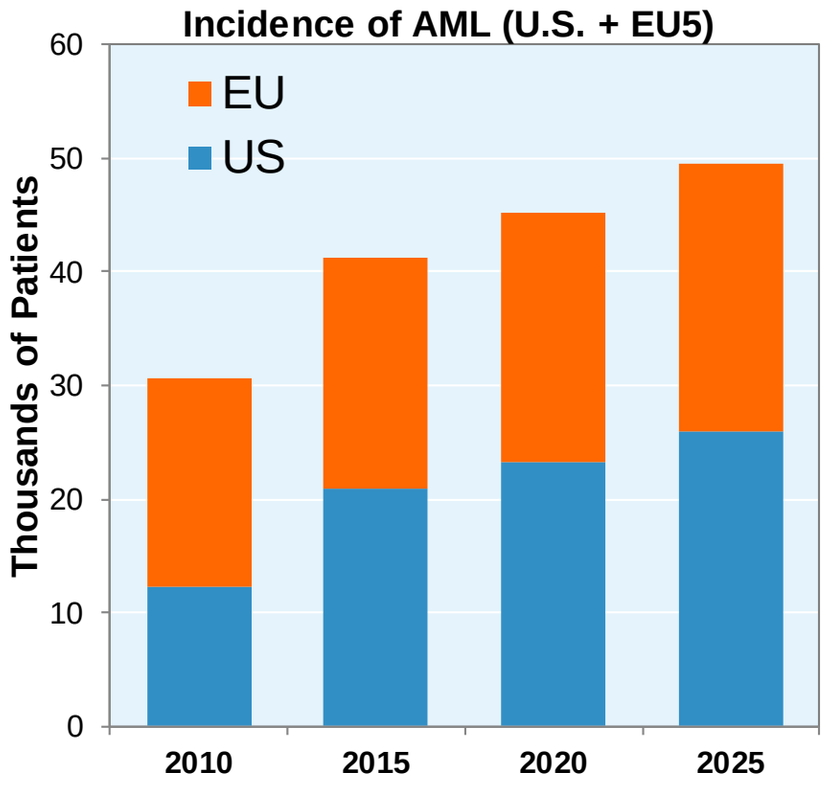
Relapsed/Refractory AML

- Novel-novel combination Phase 1 studies

Solid Tumors

- AG-120 Phase 3 cholangiocarcinoma
- AG-120 and AG-881 Phase 1 glioma expansion
- Glioma development strategy

Incidence of AML Rising in U.S. and EU5 with Aging Population



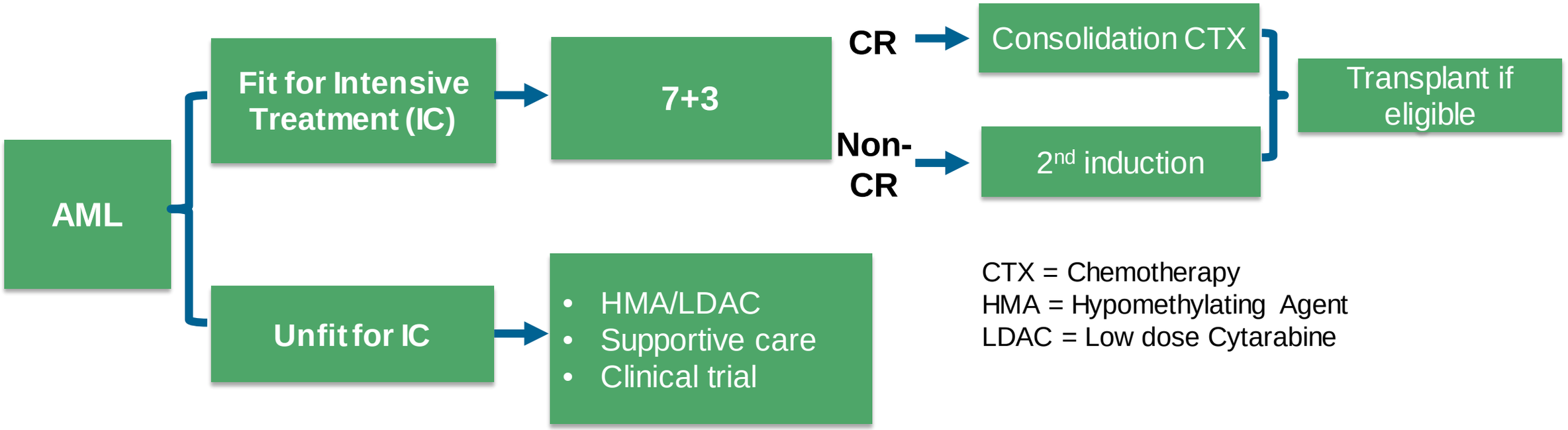
- Worldwide incidence of AML is growing in step with an aging population
- ~65% of incident patients in the U.S. and EU are 65 years of age or older
- It is estimated that ~15-23% of patients with AML will have an IDH mutation

Acute Myeloid Leukemia (AML)		
IDH1m frequency	IDH2m frequency	5-year overall survival
6-10%	9-13%	20-25%

Multiple sources including market research SEER

Sources:
1) American Cancer Society: Cancer Facts and Figures
2) Visser et. Al. Incidence, survival and prevalence of myeloid malignancies in Europe. Eur J Cancer. 2012 Nov;48(17):3257-66
3) Epiphany Partners Epic Oncology
4) Decision Resources

Shifting the Treatment Paradigm for AML with Precision Medicine



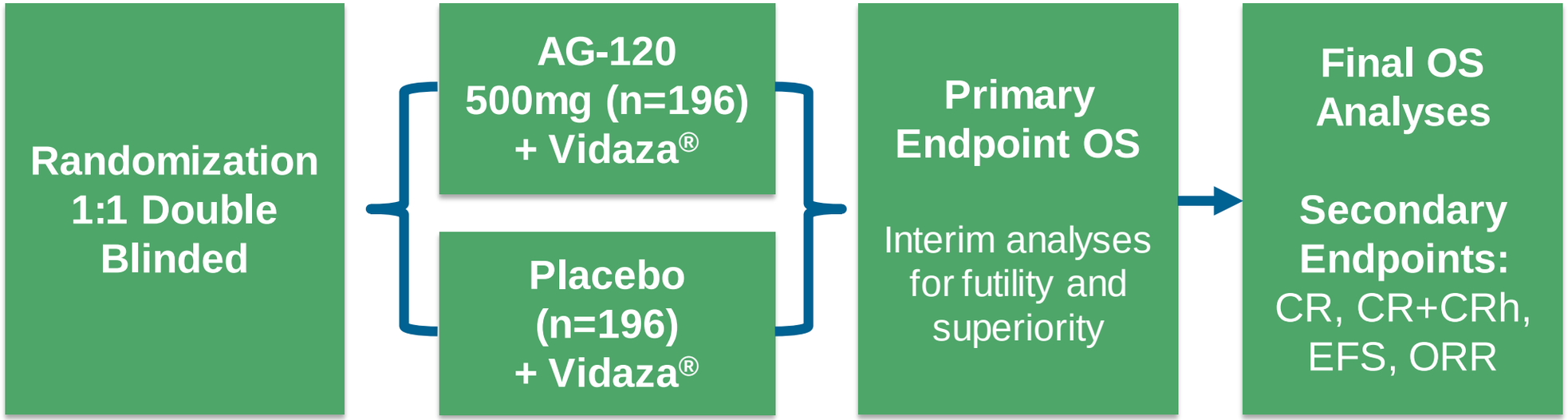
CTX = Chemotherapy
HMA = Hypomethylating Agent
LDAC = Low dose Cytarabine

Long-term goal: treatment across multiple lines with an IDHm inhibitor

Advancing AG-120 into Frontline Setting

AGILE
AGios study for IDH1 mutation in acute myeloid LEukemia

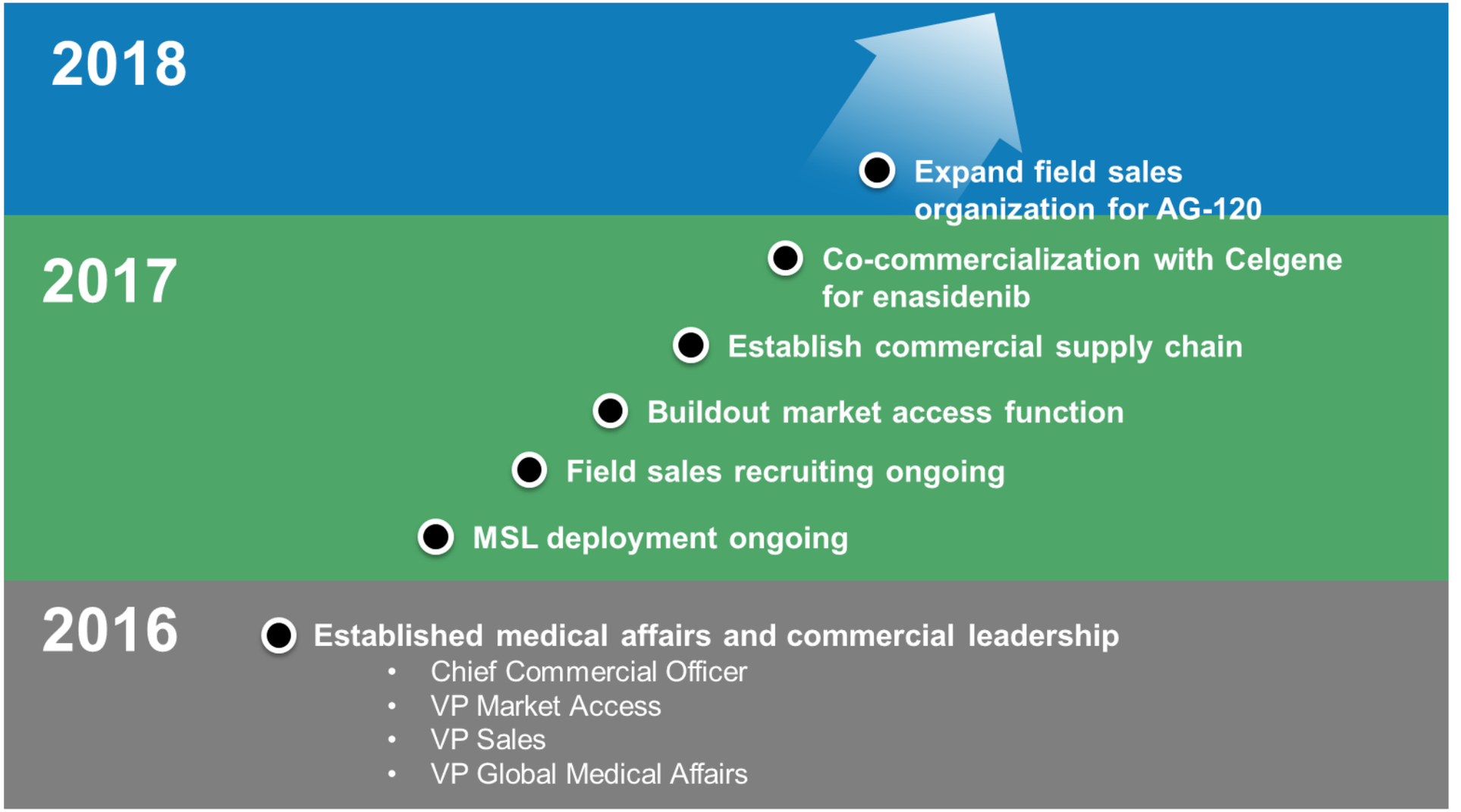
Global Phase 3 Frontline IC-Ineligible IDH1m AML



IC = intensive chemotherapy
Vidaza® is a registered trademark of Celgene Corporation

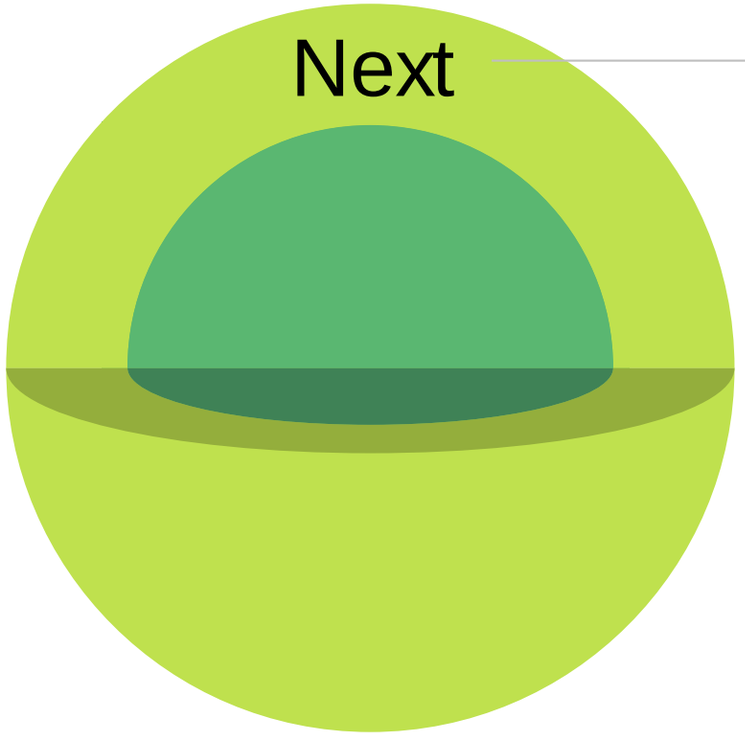
Trial on track for 1H 2017 initiation

Building World-Class Commercial Capabilities for IDH Launches



Our Vision for IDHm Inhibitors

A Roadmap for Speed and Breadth



Frontline AML

- AG-120 + Vidaza® Phase 3
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Relapsed/Refractory AML

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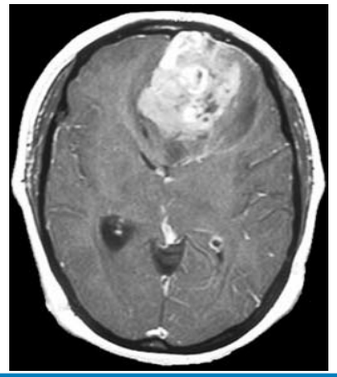
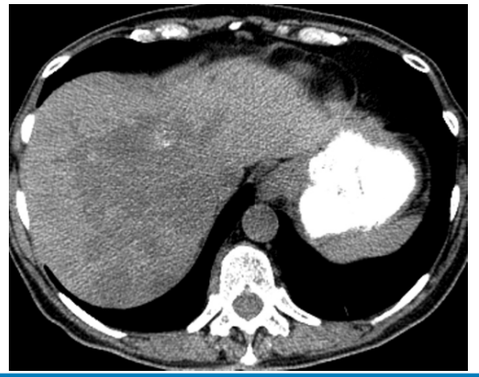
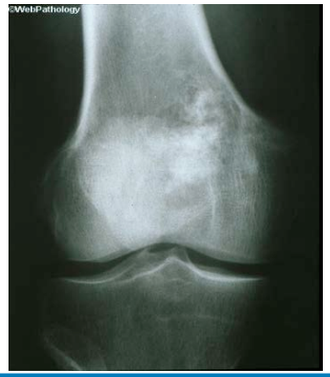
Solid Tumors

- AG-120 Phase 3 cholangiocarcinoma
- AG-120 and AG-881 Phase 1 glioma expansion
- Glioma development strategy

Treating Solid Tumors with an IDH1m Inhibitor







	Glioma	Intrahepatic Cholangiocarcinoma (IHCC)	Chondrosarcoma
	Low grade and 2^{ary} GBM	Bile ducts	Cartilage
Incidence (cases/year U.S.)	5K	2K – 4K	700 – 1000
IDH1m frequency	68-74%	11-24%	40-52%
Treatment options	Surgery, XRT Chemotherapy	Surgery, Chemotherapy Liver transplantation	Surgery, XRT Chemotherapy
5-year OS	~32-68%*	~9%	~10-90%

Other solid tumor types include colon, melanoma, lung, ovarian.
Multiple sources, including market research and SEER. Estimates will continue to evolve with additional future data
*excludes primary GBM

Registration-Enabling Phase 3 Cholangiocarcinoma Study

ClarIDHy

Global Phase 3 Previously Treated IDH1m Cholangiocarcinoma

2:1 Double Blind Randomization (n=186)

- **AG-120 Arm 500mg**
- **Placebo Arm**

Primary Endpoint: PFS

Crossover at time of progression

Secondary Endpoints: OS, ORR, safety, QoL

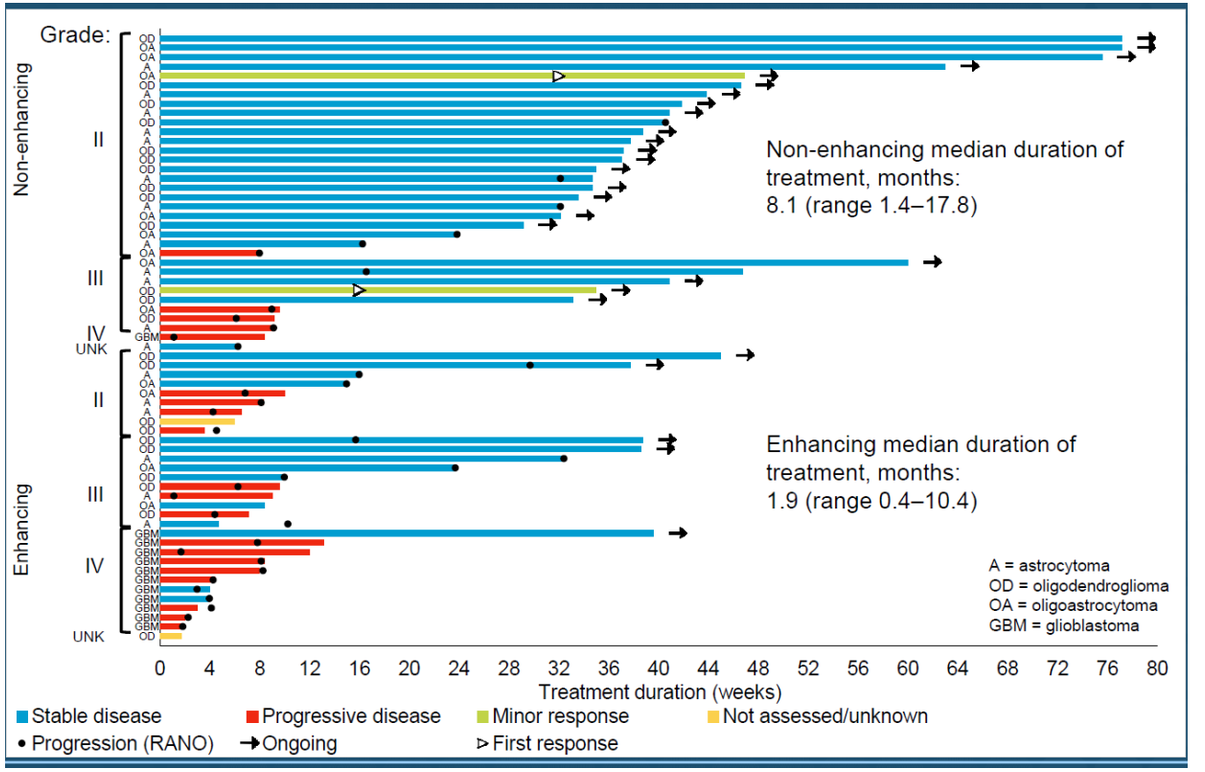
Trial Initiated in December 2016

Encouraging Data with AG-120 Supports Clinical Development of IDH1m Inhibitor in Glioma

AG-120

IDH1m Inhibition

→ Phase 1 Dose-Escalation and Expansion (Completed)



AG-881

High CNS Penetration, pan-IDHm Inhibition

→ Phase 1 Dose-Escalation (Ongoing) → Potential Expansion

AG-120 Data Presented at SNO 2016

IDH

PKR

RESEARCH

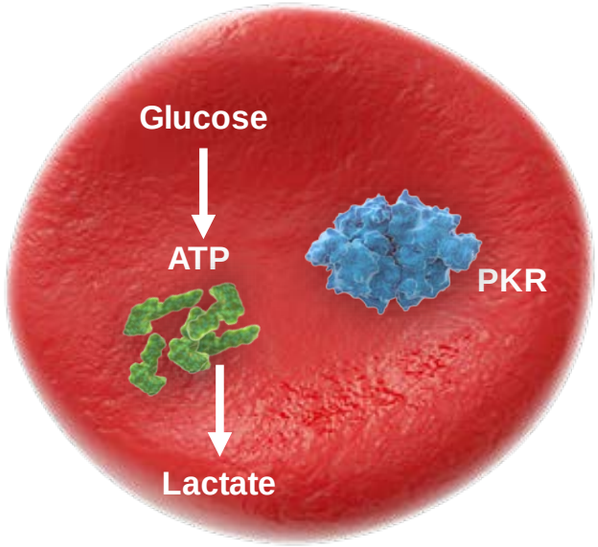
PK Deficiency Is a Rare Genetic Disease that Affects Red Blood Cells

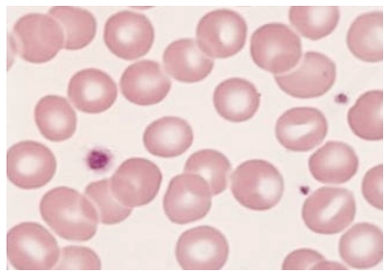
Rare genetic disease of erythrocyte pyruvate kinase

- 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]

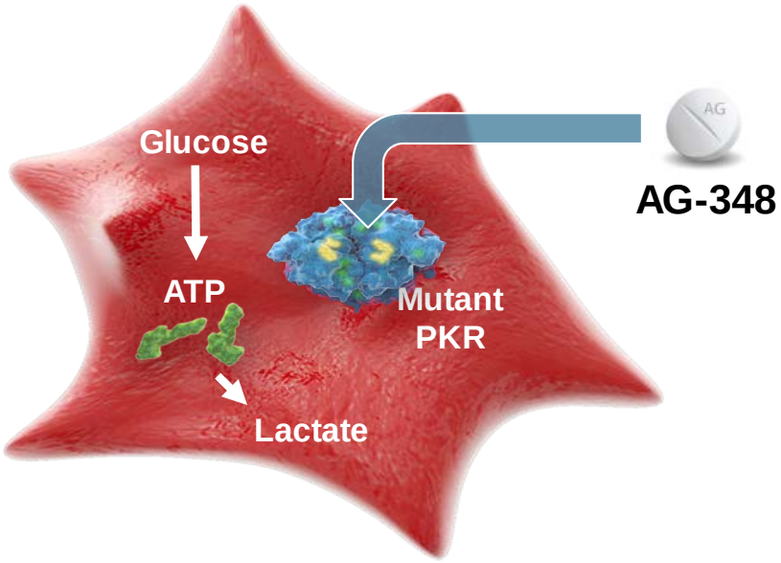
PKR regulates a crucial step in red blood cell metabolism and when mutated causes premature death of these cells

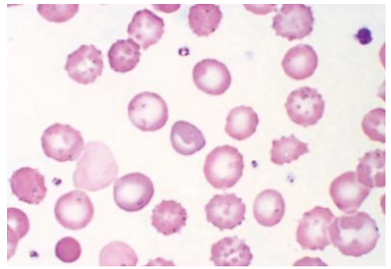
Healthy





PK Deficiency

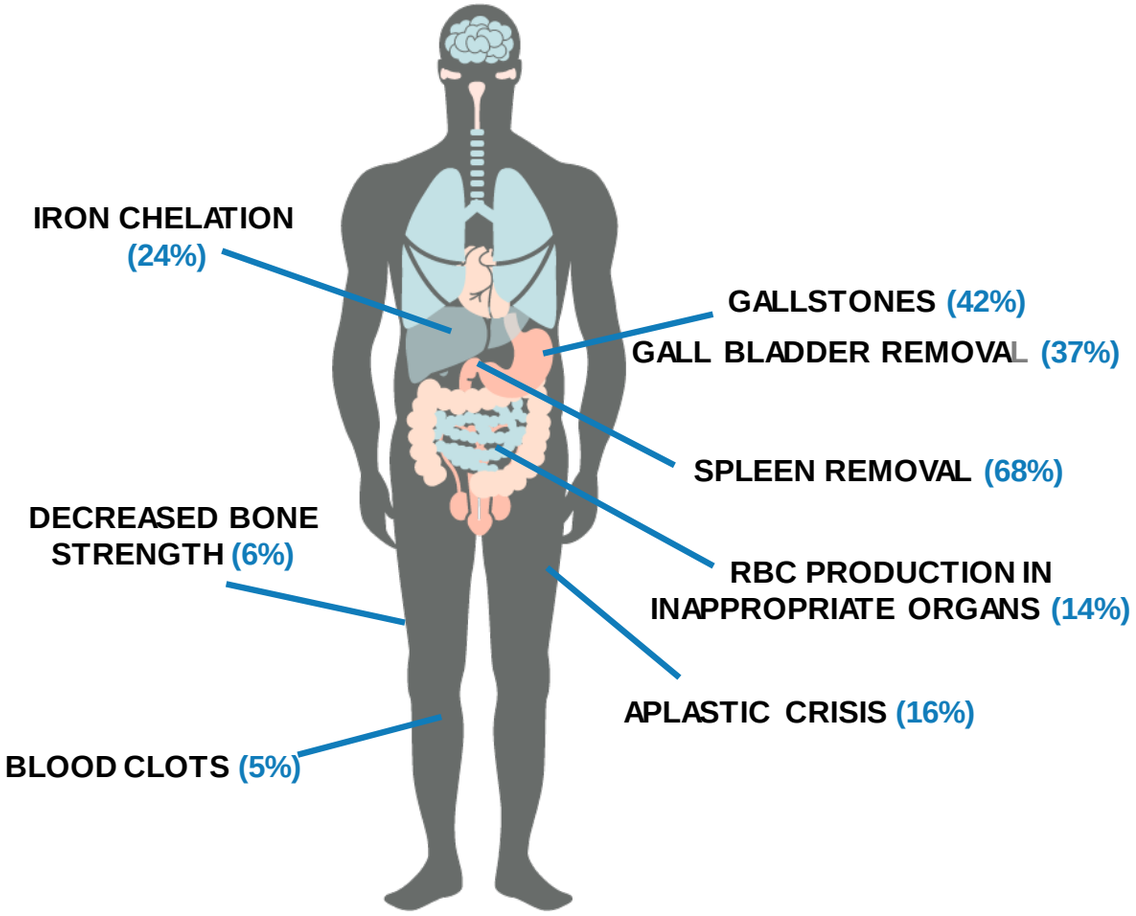




Grace R et al. *Am J Hematol* 2015;90(9):825-30; [1]Mohrenweiser HW *PNAS* 1981;78(8):5046-50; [2]Carey PJ et al. *Blood* 2000;96(12):4005-6; [3]Beutler E & Gelbart T *Blood* 2000;95(11):3585-8; [4]deMedicis et al. *Hum Hered* 1992;42(3):179-83

PK Deficiency Is a Lifelong Disease with Only Supportive Treatments

Disease Burden



	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

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

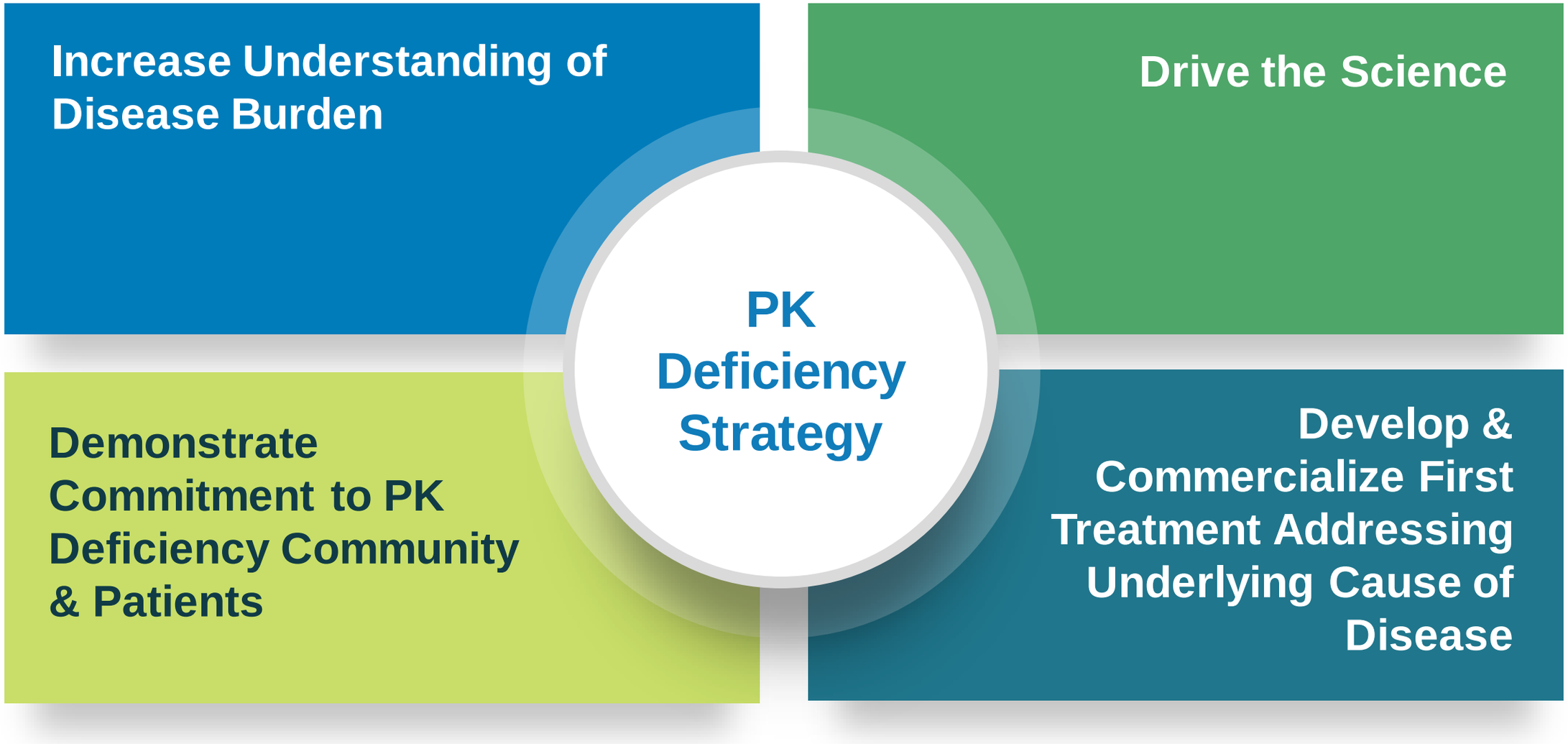
Quality of Life Impact Weighs Heavily for Both Patients & Families

"If I say I'm tired, people think I need more sleep... I have fatigue so intense that it wakes me up at night. How do you get someone to understand that?!"

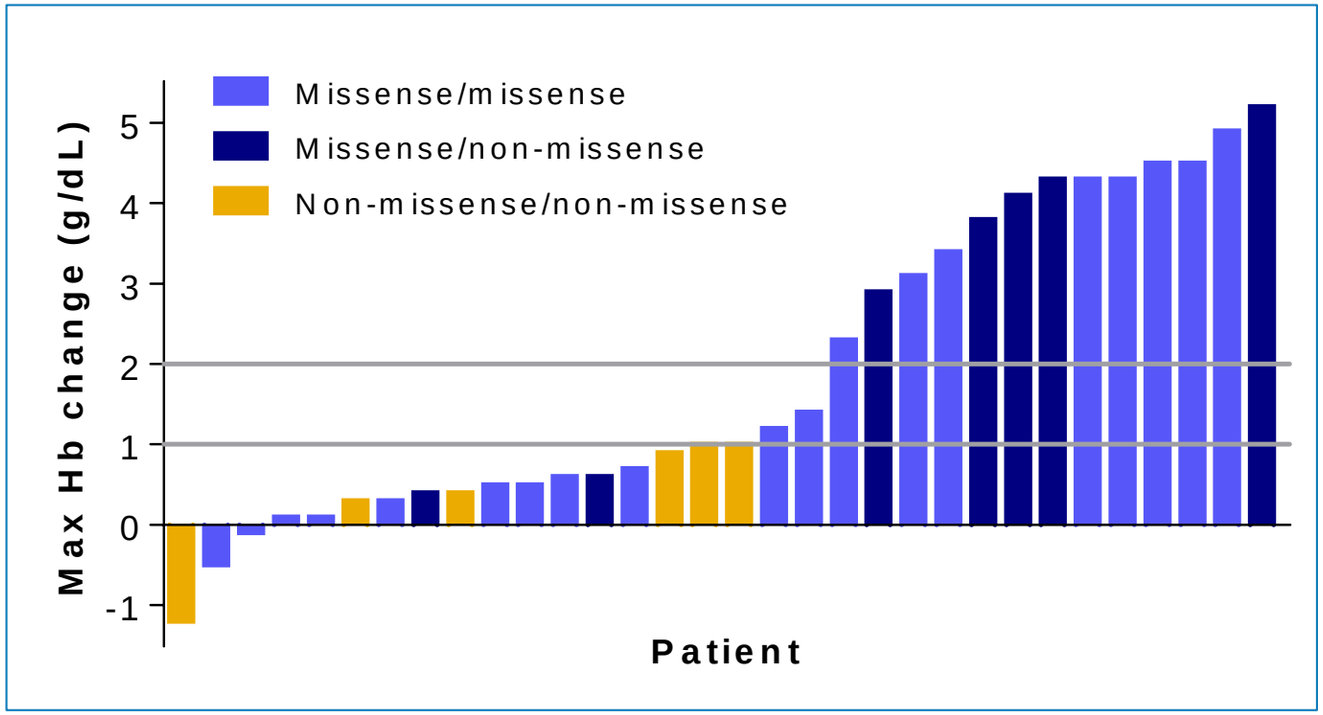
*"Think of a day when you are sick with a cold. That is me on my best day."**

*Quotes are from actual PK deficiency patients.

Agios Leadership in PK Deficiency



Compelling Proof-of-Concept for AG-348, the First Disease Modifying Therapy for PK Deficiency



52 patients enrolled;
17 completed first 24 weeks, 15 in extension

DRIVE PK Learnings
Robust hemoglobin increases in 15 / 32 patients; 15 / 26 patients with 1 or more missense mutation
Responses are rapid and sustained; median time to response of 1.4 weeks
Majority of responders seen at doses ≤50 mg BID and as low as 5 mg QD
Well-tolerated beyond six months of dosing

Data presented at ASH 2016

Key Considerations for AG-348 Pivotal Trial Design

Design Element	Considerations	Rationale
Patient Population	• Transfusion dependent adult (TD) • Non-Transfusion dependent adult (NTD)	• Goal to treat all adult patients
Size	• ~100 patients	• Rare disease
Dose	• Dose titration up to optimal hemoglobin response	• Majority of responders seen at doses ≤50 mg BID and as low as 5 mg QD
Endpoints	• Hemoglobin response (NTD) • Reduction in transfusion frequency (TD) • Patient-reported outcomes (PRO)	• Establish clinical benefit
Control	• Placebo controlled	• Evaluate PRO

Expect to initiate pivotal study in 1H 2018

IDH

PKR

RESEARCH

Agios' Scientific Research Platform

DYSREGULATED METABOLISM

CANCER METABOLISM

- Inhibit key enzymes in ***cancer cell*** specific metabolic pathways to disrupt tumor cell proliferation and survival

RARE GENETIC DISEASES

- Restore defective metabolic pathways in ***disease cells*** that cause rare genetic disorders of metabolism

METABOLIC IMMUNO-ONCOLOGY

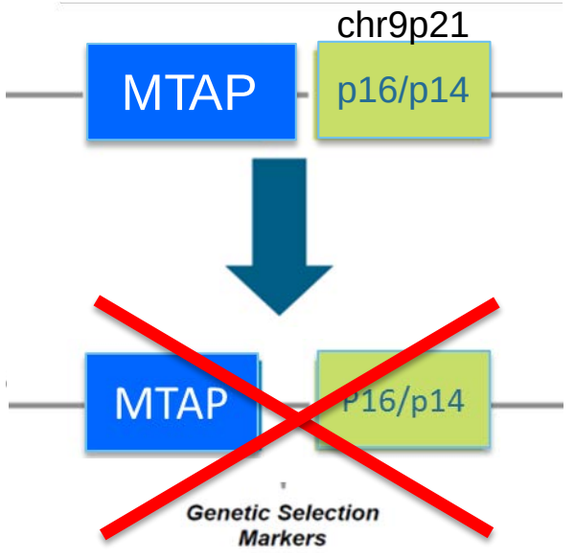
- Alter the metabolic state of ***immune cells*** to enhance the body's anti-tumor response

RESEARCH PLATFORM

Development Candidate for MTAP Pathway Selected

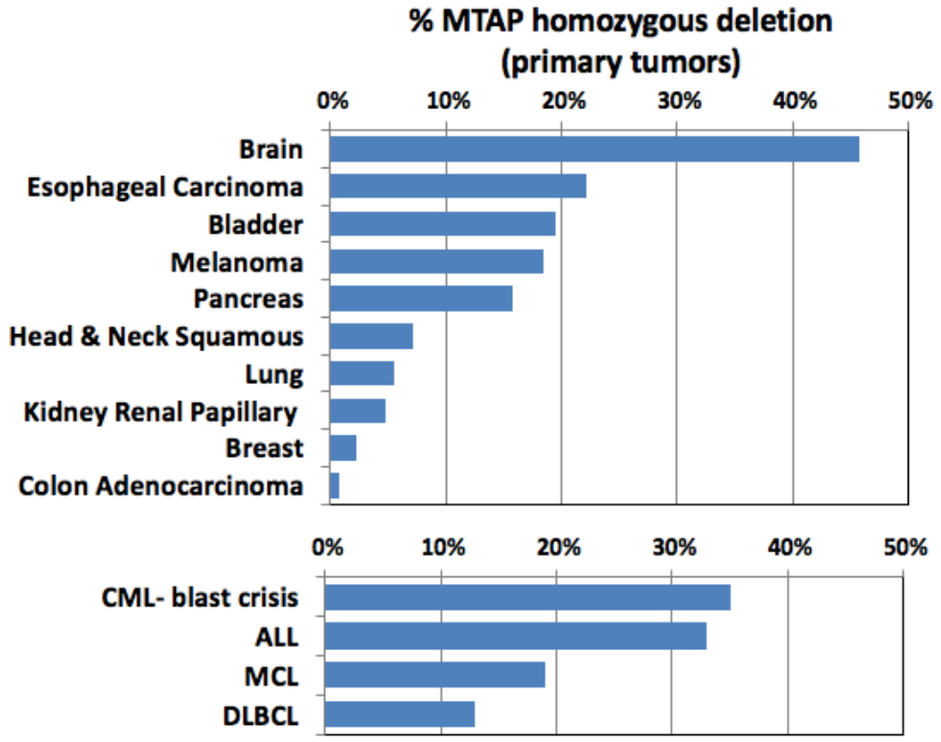
IND Expected by Year-End

Deletion of metabolic gene adjacent to tumor suppressor p16/p14



- p16/p14 tumor suppressor locus deleted in 15% of all cancers
- Metabolic gene, MTAP, is adjacent to p16/p14 & typically co-deleted

~75,000 new patients/year in U.S. with MTAP deletion across many indications



MTAP-deleted tumors constitute a large, genetically defined patient population

2017 – 2018

Commercial Stage Biopharmaceutical Company

2	4+	3+	3	450+	100%
approved precision medicines in AML	clinical-stage molecules	pivotal trials (IDH, PKR)	areas of research expertise	employees	committed to helping patients

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Thank You

Founder's Day Retreat 2016