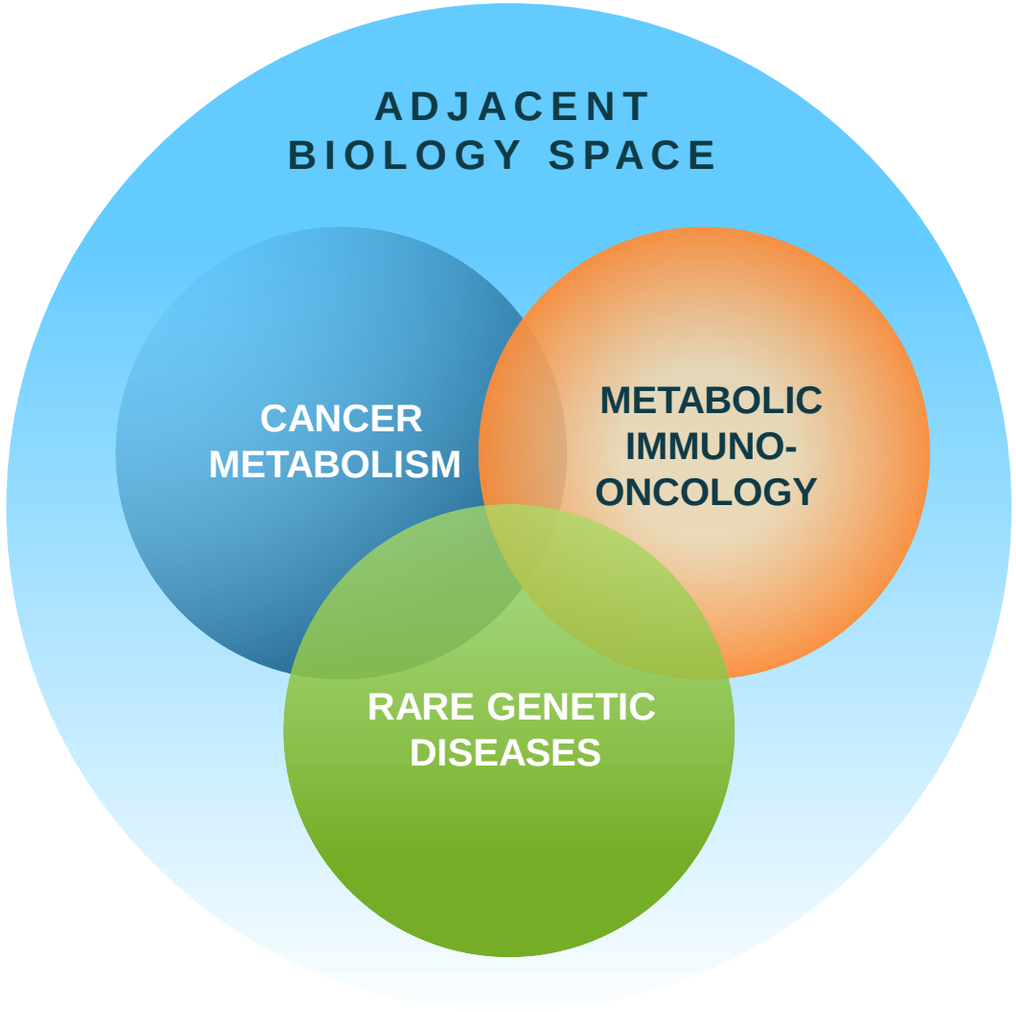

# Agios Investor Presentation

August 2018

# 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 IDHIFA®, TIBSOVO®, AG-881, mitapivat (AG-348), AG-270 and AG-636; the potential benefits of Agios' product candidates; its key milestones for 2018; 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 benefit of its strategic plans and focus. The words "anticipate," "believe," "could," "estimate," "expect," "hope," "intend," "may," "milestone," "path", "plan," "possible," "potential," "predict," "prepare", "project," "strategy," "will," "would," 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 are 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 CStone Pharmaceuticals; 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.

# 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.*

# Agios' Scientific Platform Demonstrates Remarkable, Reproducible Productivity

## DISCOVERY

**$50-60M**
INVESTED IN DRUG DISCOVERY ANNUALLY

## SCIENCE

**40+**
PEER-REVIEWED PUBLICATIONS

## CULTURE

**450+** EMPLOYEES

**1** **VISION**

**10+**
CLINICAL TRIALS IN
**6** DISEASES

**1,000+**
PATIENTS TREATED IN CLINICAL TRIALS

**6** INDs

**2** MEDICINES APPROVED

**+**

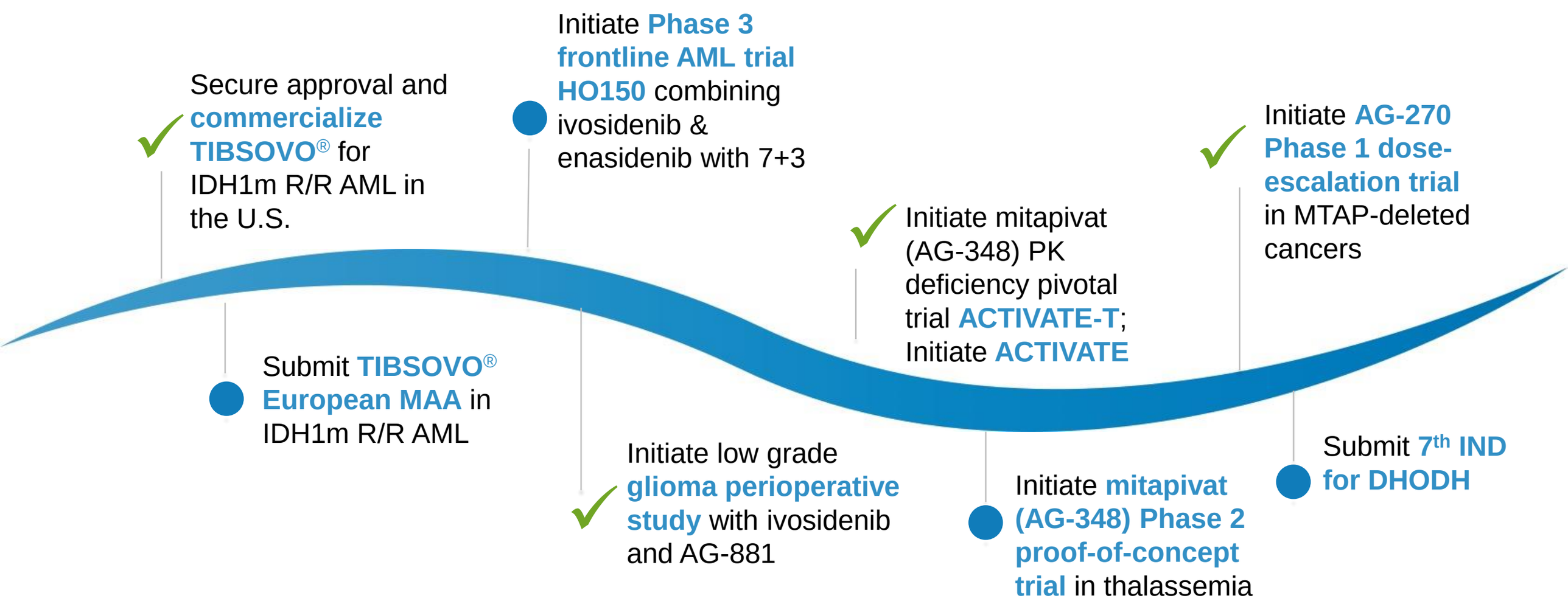
**3** ADDITIONAL COMPOUNDS IN CLINICAL DEVELOPMENT

# Current Clinical Portfolio Has Potential to Benefit Large Number of Patients

| | |
|---|---|
| ACUTE MYELOID LEUKEMIA | ~10,000 IDHm Patients<br>AML Opportunity ~$2B |
| CHOLANGIO-CARCINOMA | ~3,000 IDH1m Patients |
| LOW GRADE GLIOMA | ~9,000 IDH1m Patients |
| PYRUVATE KINASE DEFICIENCY | ~3,000 to ~8,000 Patients |
| MTAP-DELETED TUMORS | >100,000 MTAP Deletion Patients |

**Oncology patient numbers represent annual U.S. and EU incidence; PK deficiency represent U.S. and EU prevalence**

# 2018 Key Milestones



# Expected Fourth Quarter Clinical Data Presentations

**Key Abstracts Submitted to ASH**

**Updated data in IDHm newly diagnosed AML from the Phase 1 combination trial of ivosidenib or enasidenib with standard-of-care intensive chemotherapy**

**Updated data in MDS from the Phase 1 study of ivosidenib in IDH1m hematologic malignancies**

**Updated data in untreated AML from the Phase 1 study of ivosidenib in IDH1m hematologic malignancies**

# Our Pipeline

| CLINICAL PROGRAMS | INDICATION | DRUG DISCOVERY | EARLY STAGE CLINICAL DEVELOPMENT | LATE STAGE CLINICAL DEVELOPMENT | APPROVED | PRIMARY COMMERCIAL RIGHTS |
|---|---|---|---|---|---|---|
| **IDHIFA®** ***enasidenib*** (IDH2m Inhibitor) | R/R AML | | | | ● | agios Celgene Agios U.S. Co-promotion and Royalty |
| | Frontline AML | | | ● | | |
| **TIBSOVO®** ***ivosidenib*** (IDH1m Inhibitor) | R/R AML | | | | ● | agios |
| | Frontline AML | | | ● | | |
| | Cholangio | | | ● | | |
| | Glioma | | ● | | | |
| **AG-881** (pan-IDHm Inhibitor) | Glioma | | ● | | | agios |
| **mitapivat** (PK (R) Activator) | PK Deficiency | | | ● | | agios |
| **AG-270** (MAT2A Inhibitor) | MTAP-deleted Tumors | | ● | | | agios Celgene |
| **RESEARCH PROGRAMS** | | | | | | |
| **AG-636 (DHODH)** | | ● | | | | agios |
| **CM Research Programs** | | ● | | | | agios |
| **RGD Research Programs** | | ● | | | | agios |
| **Metabolic IO Research Programs** | | ● | | | | agios Celgene |

# CANCER

RARE GENETIC DISEASES

RESEARCH

# IDH Mutations Across Many Tumor Types

| | |
|---|---|
| **ACUTE MYELOID LEUKEMIA (AML)** | **~20% of Patients Have IDH1 OR IDH2 Mutation**<br>**~10,000 IDHm Patients** |
| **CHOLANGIO-CARCINOMA** | **~14 % have IDH1 Mutation**<br>**~3,000 IDH1m Patients** |
| **MYELODYSPLASTIC SYNDROMES (MDS)** | **~8% have IDH1 or IDH2 Mutation**<br>**~3,000 IDHm Patients** |
| **LOW GRADE GLIOMA** | **~80% have IDH1 Mutation**<br>**~9,000 IDH1m Patients** |
| **CHONDROSARCOMAS** | **~50% have IDH1 Mutation**<br>**~900 IDH1m Patients** |

Sources: SEER. Cancer Stat Facts: AML 2015 and Epiphany EPIC oncology numbers; American Cancer Society. AML 2017.; Visser et. Al. Incidence, survival and prevalence of myeloid malignancies in Europe. Eur J Cancer. 2012 Nov;48(17):3257-66 DiNardo et al. Leukemia 2016;30(4):980-4, Amary MF et al. J Pathol 2011;224:334-43, Epiphany Partners Epic Oncology, DC National Program of Cancer Registries (NPCR); Borger DR et al. Oncologist 2012;17:72-9.; Kipp BR et al. Hum Pathol 2012;43:1552-8.; Goyal L et al. Oncologist 2015;20:1019-27.SEER. Cancer Stat Facts, CBTRUS (Central Brain Tumor Registry in the US); Neurosurg Focus. 2015 Jan; 38(1): E6.

**Patient numbers represent annual U.S. and EU incidence**

# Multiple Opportunities Across IDHm Hematologic and Solid Cancers Originating from Agios Research Platform

## ACUTE MYELOID LEUKEMIA

**IDH2m R/R**
***IDHIFA® Approved***

**IDH1m R/R**
***TIBSOVO® Approved***

**IDH1m Frontline Non-IC**
***Ivosidenib + Aza Phase 3 (AGILE) Ongoing***

**IDHm Frontline IC-Eligible**
***Ivo/Ena + 7+3 Phase 3***
***Q4 2018 Start***

**IDHm Frontline Non-IC**
***Ivo/Ena + Aza Phase 1/2 Ongoing***

**IDHm Frontline IC-Eligible**
***Ivo/Ena + 7+3 Phase 1b Ongoing***

## CHOLANGIOCARCINOMA

**IDH1m R/R**
***Ivosidenib Phase 3 (ClarIDHY) Ongoing***

**IDH1m R/R**
***Ivosidenib Phase 1***
***Enrollment Complete***

## LOW GRADE GLIOMA

**IDH1m**
***Ivosidenib & AG-881***
***Perioperative Study Ongoing***

**IDH1m**
***Ivosidenib***
***Phase 1 Enrollment Complete***

**IDH1m**
***AG-881***
***Phase 1 Enrollment Complete***

## OTHER INDICATIONS

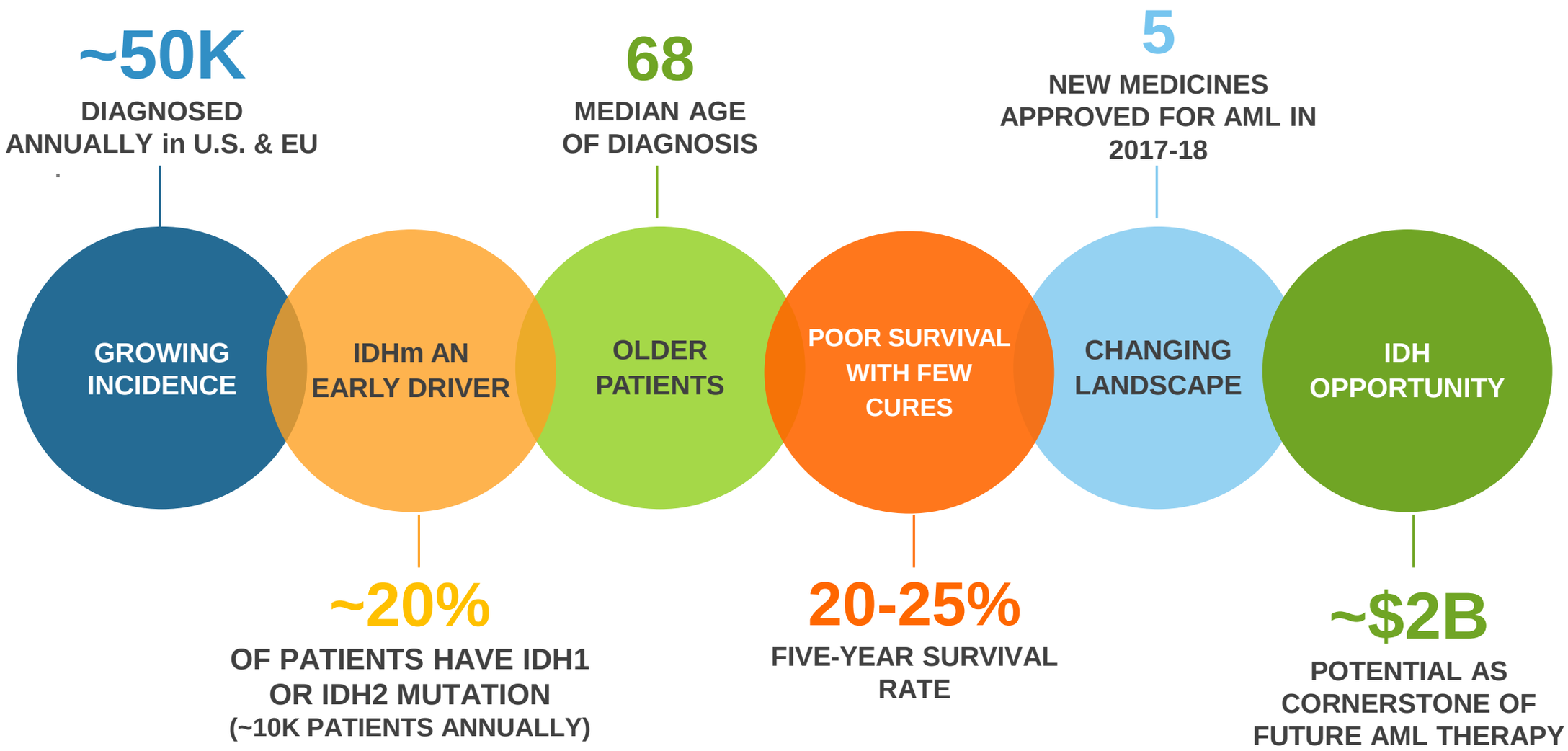
### MYELODYSPLASTIC SYNDROMES

***IDHm R/R***
***Ivosidenib Phase 1***
***Enrollment Complete***

### CHONDROSARCOMAS

***IDH1m R/R***
***Ivosidenib Phase 1***
***Enrollment Complete***

# AML Landscape on the Brink of a Therapeutic Tidal Shift




Sources: SEER. Cancer Stat Facts: AML 2015 and Epiphany EPIC oncology numbers; American Cancer Society. AML 2017.; Visser et. Al. Incidence, survival and prevalence of myeloid malignancies in Europe. Eur J Cancer. 2012 Nov;48(17):3257-66; Thomas ED, N Engl J Med. 1979 Mayer, N Engl J Med. 1994, Fernandez H,N Engl J Med, 2009; Kumar C. Genetic Abnormalities and Challenges in the Treatment of Acute Myeloid Leukemia. *Genes Cancer*. 2011; 2:95–107; AML O/S: Klepin, et al, JCO, 32, 2014

# Now Approved in IDH1m Relapsed/Refractory AML


**TIBSOVO is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test.**

# TIBSOVO® USPI Highlights*

First-in-class, oral, targeted inhibitor of mutant IDH1 protein

## Efficacy Data (n=174)

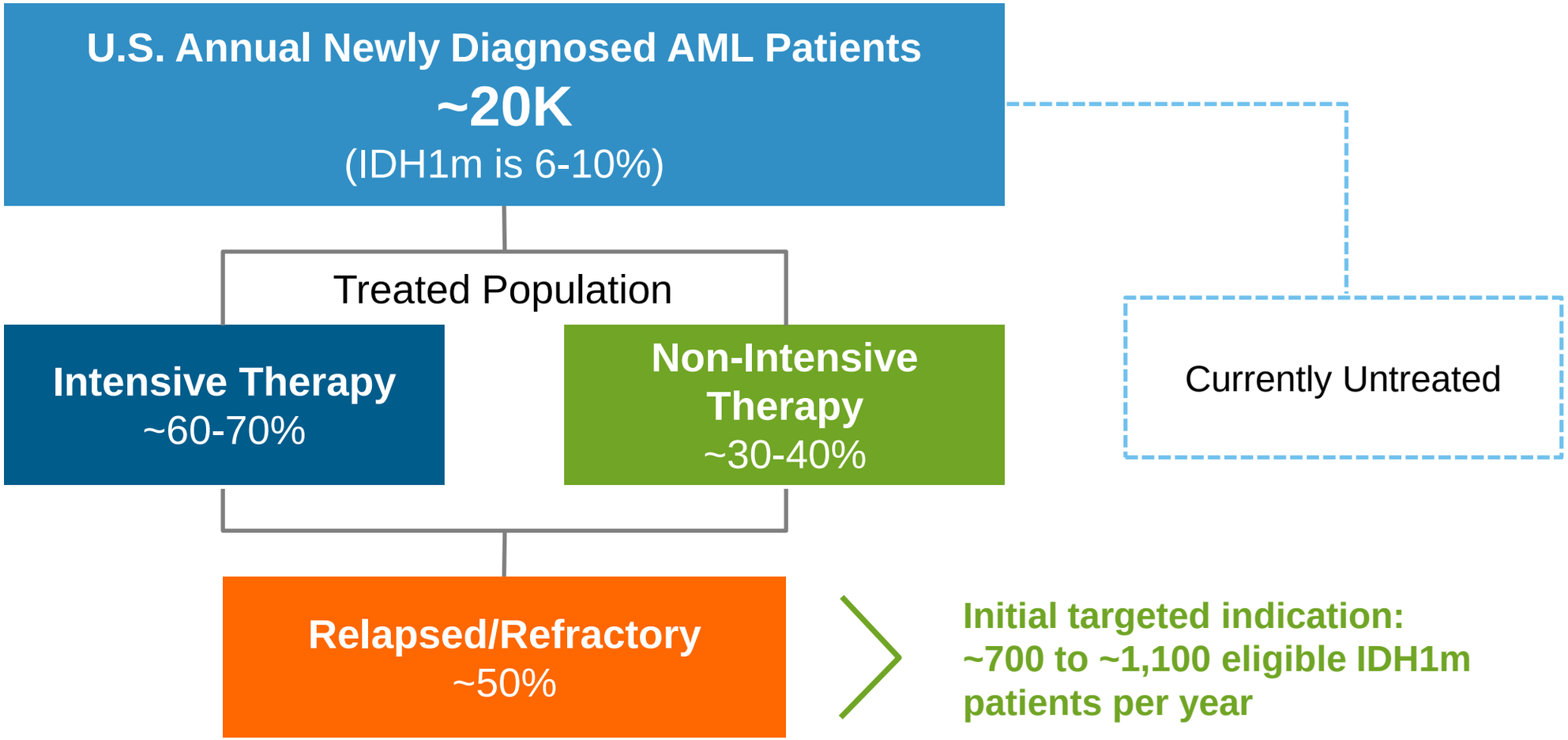
- CR/CRh statistics
  - Rate: 32.8%
  - Median duration: 8.2 months
  - Median time to first response: 1.9 months
  - Median time to best response 2.0 months
- Transfusion independence
  - 37.3% of patients became transfusion independent during any 56-day post-baseline period
  - 59.4% of patients independent at baseline remained independent during any 56-day post-baseline period
- 12% of patients went on to stem cell transplant following TIBSOVO® treatment

## Safety Data (n=179)

- The TIBSOVO® label contains a boxed warning for differentiation syndrome, which can be fatal if not treated
  - 19% of patients experienced differentiation syndrome (all Grades)
- QTc interval prolongation and Guillain-Barre Syndrome occurred in patients treated with TIBSOVO®
- Monitor drug-drug interactions with TIBSOVO.
- Most frequent serious adverse reactions (≥5%): differentiation syndrome (10%), leukocytosis (10%) and QT prolongation (7%)
- Median duration of exposure: 3.9 months

* The full prescribing information can be found on our website at agios.com.

# U.S. AML Epidemiology and Treatment Approach – IDH1 Opportunity




Sources: 1. National Cancer Institute. https://seer.cancer.gov/statfacts/html/amyl.html. Accessed December 7, 2017. 2. DiNardo CD, et al. Poster presented at: American Society of Hematology Annual Meeting & Exposition; December 9-12, 2017; Atlanta, GA. 3. Walter RB, et al. *Leukemia*. 2015;29(2):312-320.

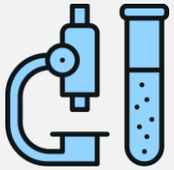
# IDHIFA® Launch Metrics Are on Track

| Sales | Diagnostic Testing | Prescriber Base | Awareness |
|---|---|---|---|
| **Early IDHIFA® Success** | | | |
| 2017 sales **$20M** | IDH2m testing at **~50% as of October** | **>250** unique prescribers | IDHIFA® awareness of **~50% as of October** |
| **IDHIFA® Launch Metrics Update** | | | |
| 2018 Q2 sales **$17M** | IDH2m testing at **~70% as of January** | >**300** unique prescribers | IDHIFA® awareness of **~60% as of January** |

Revenues reported by Celgene; Market research as of Oct. 2017 and January 2018; Agios estimates

# Strategic Imperatives for the TIBSOVO® Launch

**Physicians test for IDH1m**



**TIBSOVO® is recognized as the best option for IDH1m+ R/R AML**

TIBSOVO® (ivosidenib) tablets

**Patients have access to TIBSOVO®**

# Clinical Development of IDHm Inhibitors Spans All Treatment Lines to Become Cornerstone of AML Treatment

**INTENSIVE CHEMO (IC)**
**~60-70% of AML Patients**

**NON-IC TREATMENT**
**~30-40% of AML Patients**

**HO150 7+3 PHASE 3 PLANNED**

**BROAD IST SUPPORT**

**IC INDUCTION**

**CONSOLIDATION**

**TRANSPLANT**

**MAINTENANCE**

**NON-IC TREATMENT**

AGILE
AGIos study for IDH1 mutation in acute myeloid LEukemia

**ONGOING**

**BROAD IST SUPPORT**

**RELAPSED / REFRACTORY TREATMENT**

IDHIFA® (enasidenib) tablets 100mg • 50mg **APPROVED**

TIBSOVO® (ivosidenib) tablets **APPROVED**

**BROAD IST SUPPORT**

Source: SEER. Cancer Stat Facts: AML 2015

# Potential for IDHm inhibitors in AML Frontline Setting: Encouraging Data from Ongoing Phase 1 Combination Trials

## Ivosidenib plus 7+3 n=32

- Median age 60.5 years
- 69% (n=22) de novo AML
- Combination safe & well tolerated
- CR+ CRi/CRp rate for all patients = 77% (23 of 30)
- CR+CRi/CRp rate for de novo patients = 91% (19 of 21)

**Updated data submitted to ASH**

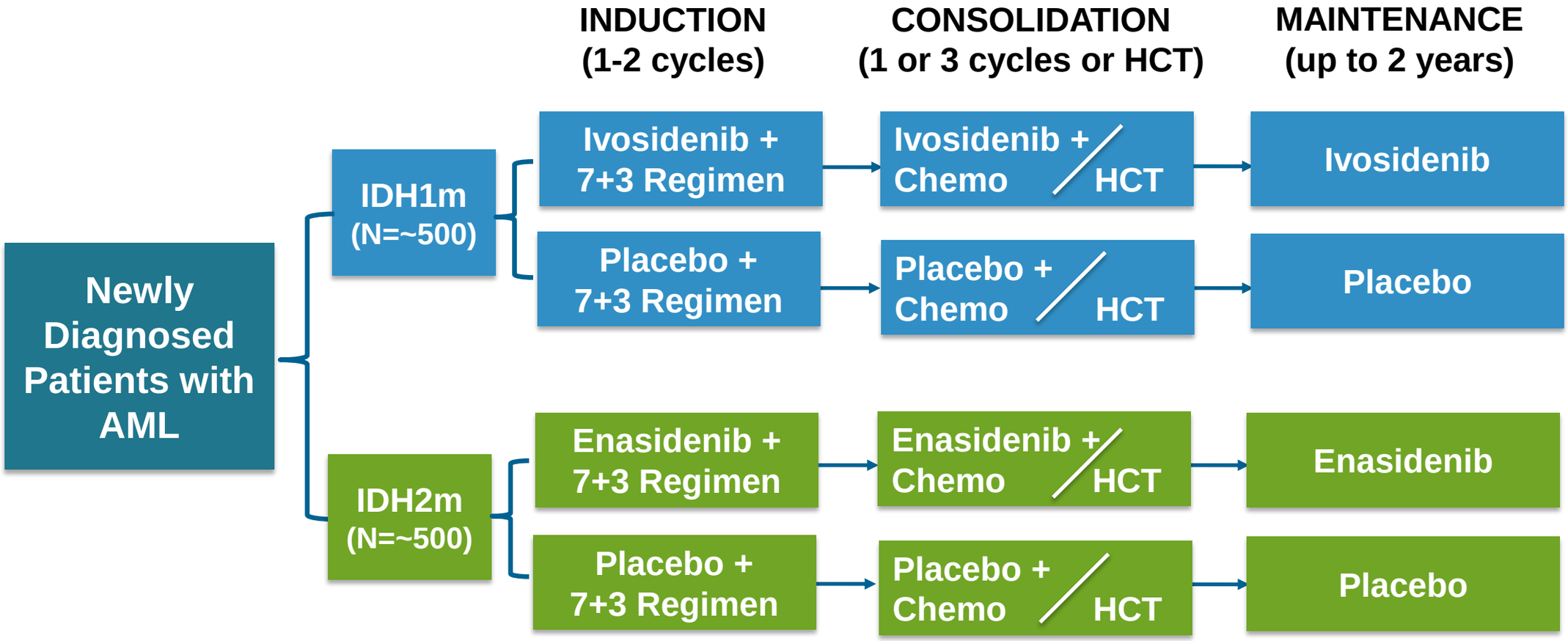
## Ivosidenib plus Azacitidine n=23

- Median age 76 years
- Combination safe & well tolerated
- 78% ORR rate (18 of 23)
- 44% CR rate (10 of 23)

**Data updated at ASCO**

Sources: 7+3 data from ASH 2017,
Aza data from ASCO 2018

# HO150 Phase 3 Intergroup Frontline AML Trial in Collaboration with Celgene Planned for Q4 2018




EFS = Event Free Survival
HCT = Hematopoietic Cell Transplantation

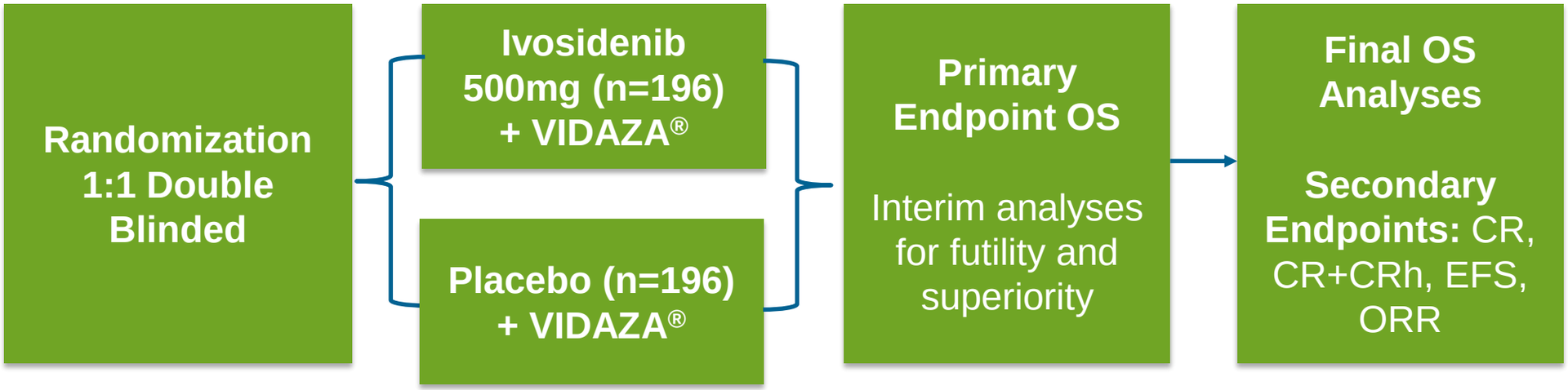
**EFS primary endpoint; sponsored by HOVON and AML-SG**

# Phase 3 Frontline AGILE Ongoing

AGIOS study for IDH1 mutation in acute myeloid LEukemia

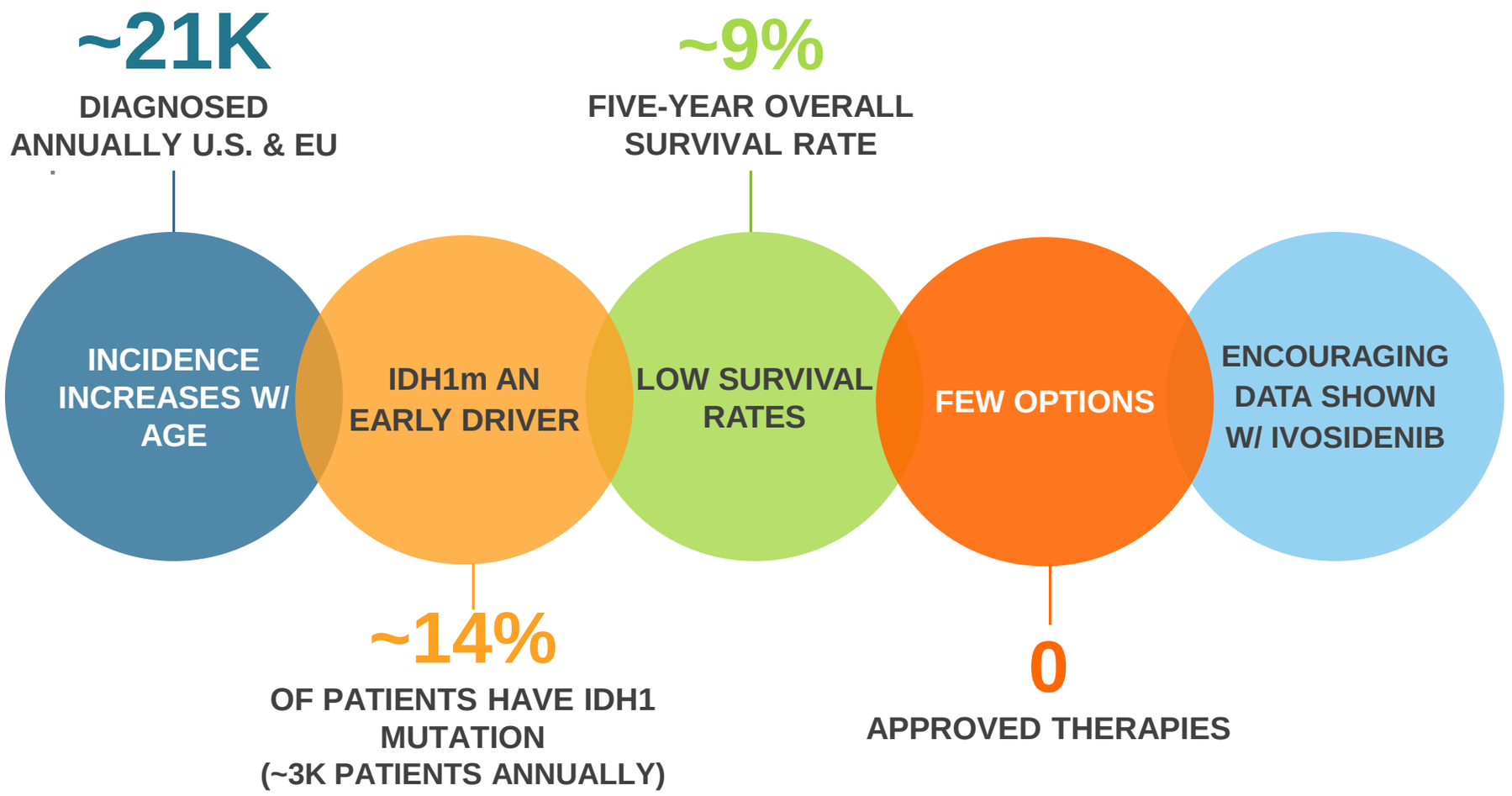
**Global Phase 3 Frontline IC-Ineligible IDH1m AML**

*Expect to complete enrollment in 2021*




ClinicalTrials.gov Identifier:NCT03173248
IC = intensive chemotherapy
VIDAZA® is a registered trademark of Celgene Corporation

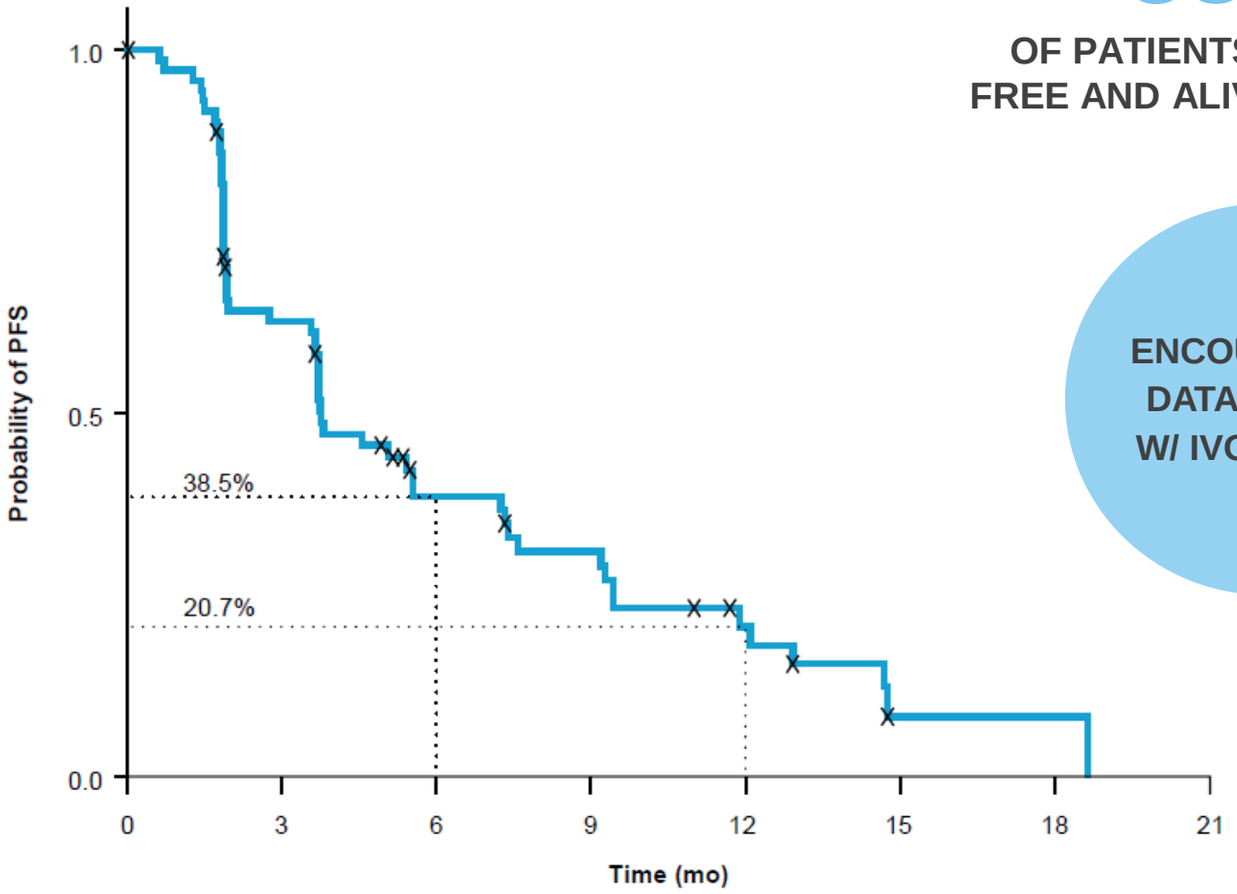
# Cholangiocarcinoma a Devastating Disease with No Approved Targeted Therapies




Sources: CDC National Program of Cancer Registries (NPCR); Epiphany Partners Epic Oncology; Decision Resources; Market Research; Borger DR et al. Oncologist 2012;17:72-9.; Kipp BR et al. Hum Pathol 2012;43:1552-8.; Goyal L et al. Oncologist 2015;20:1019-27.

# Durable Disease Control with Ivosidenib in a Phase 1 Heavily Pre-treated Population

- Ivosidenib well-tolerated in heavily pre-treated population (most common drug-related AEs: fatigue, nausea & vomiting)
- Median of 2 prior systemic therapies (range 1-5)
- Durable disease control with six month PFS rate of 38.5% and 12 month PFS rate of 20.7%; median PFS of 3.8 months




18 of 73 (25%) censored. As of March 10, 2017
Median 2 prior therapies (range 1–5)

**38.5%**

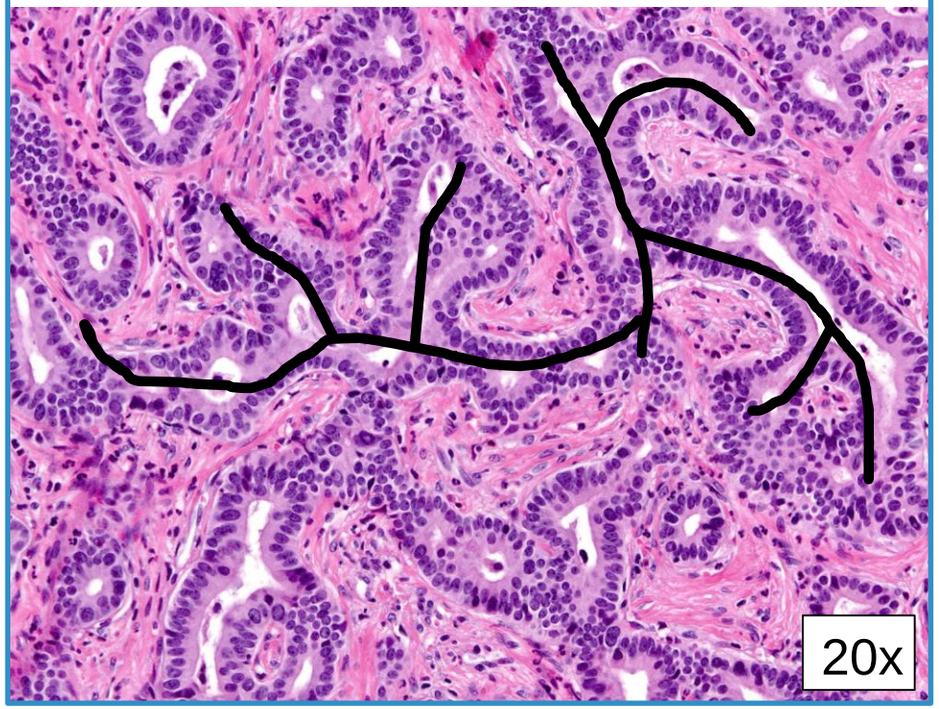
**OF PATIENTS PROGRESSION FREE AND ALIVE AT SIX MONTHS**

**ENCOURAGING DATA SHOWN W/ IVOSIDENIB**

Source: Data from ASCO 2017

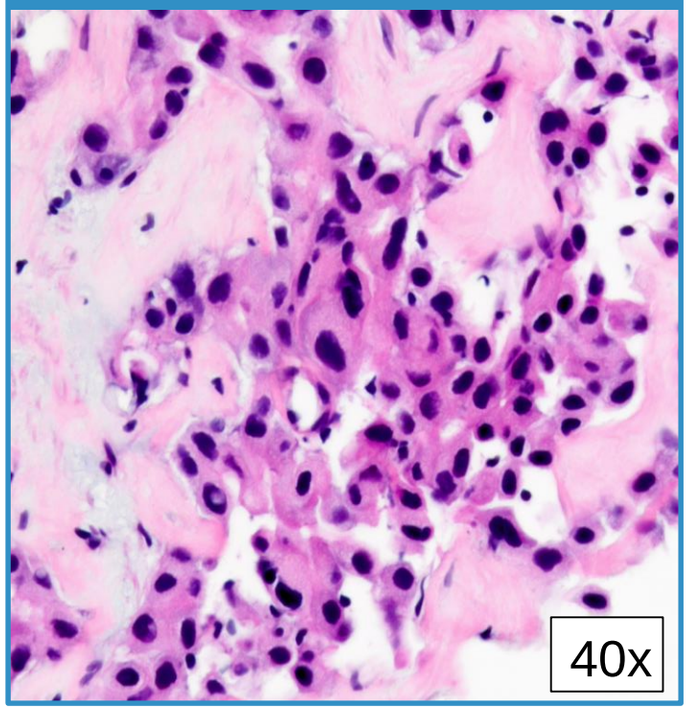
# Ivosidenib Promotes Morphologic Changes to Cholangiolar Patterns

## Cholangiolar pattern[4]



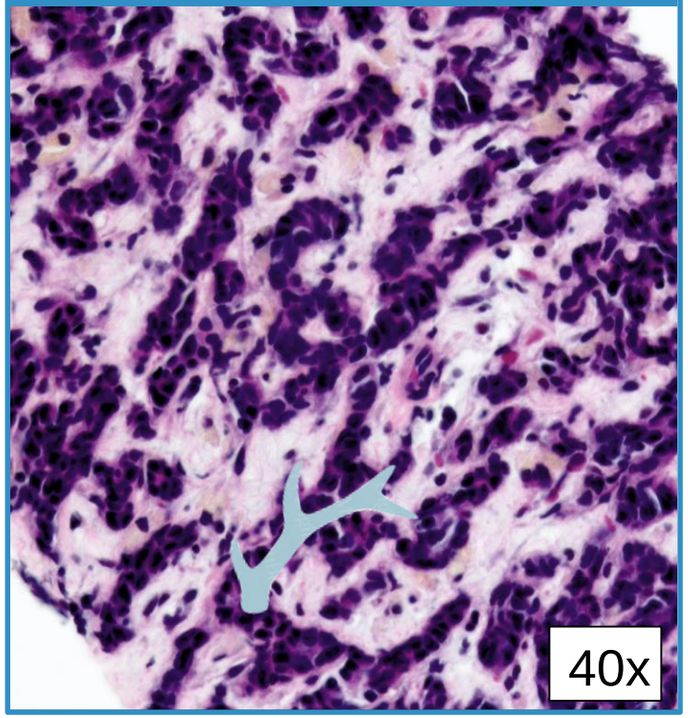

- ‘Normal’ cholangiolar pattern composed of glands in the shape of antler horns[1-3]
- Associated w/ better clinical outcomes in patients w/ ICC [1,4]

## Baseline




- Untreated IDH1m+ ICCs often show heterogeneous histoarchitecture

## Cycle 7, Day 1 (PR)




- Treatment with ivosidenib shows increased cholangiolar histology and decreased cytoplasm



Sources: 1. Liau JY et al. *Mod Pathol* 2014;27:1163-73, 2. Komuta M et al. *Hepatology* 2012;55:1876-88. 3. Komuta M et al. *Hepatology* 2008;47:1544-56, 4. V. Deshpande, unpublished data, 2017.

Data from CCF 2018

# Registration-Enabling Phase 3 Cholangiocarcinoma Study Ongoing

ClarIDHy

**Global Phase 3 Previously Treated Advanced IDH1m Cholangiocarcinoma (no more than 2 prior therapies)**

**2:1 Double Blind Randomization (n=186)**

- **Ivosidenib Arm 500mg**
- **Placebo Arm**

**Primary Endpoint: PFS**

Crossover at time of progression

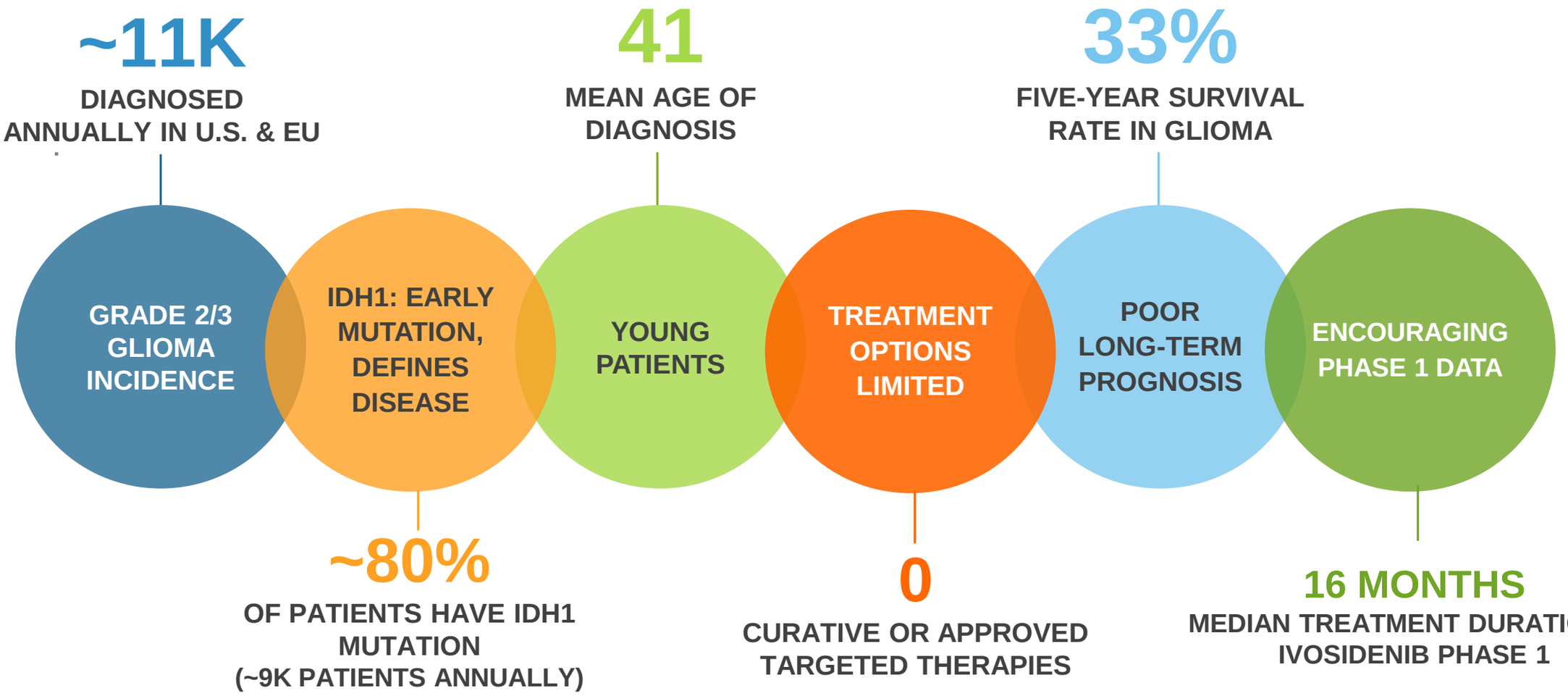
**Secondary Endpoints:** OS, ORR, safety, QoL

The study has 96% power to detect a hazard ratio of 0.5 with a one-sided alpha of 0.025

ClinicalTrials.gov Identifier: NCT02989857

**Expect to complete enrollment in 1H 2019**

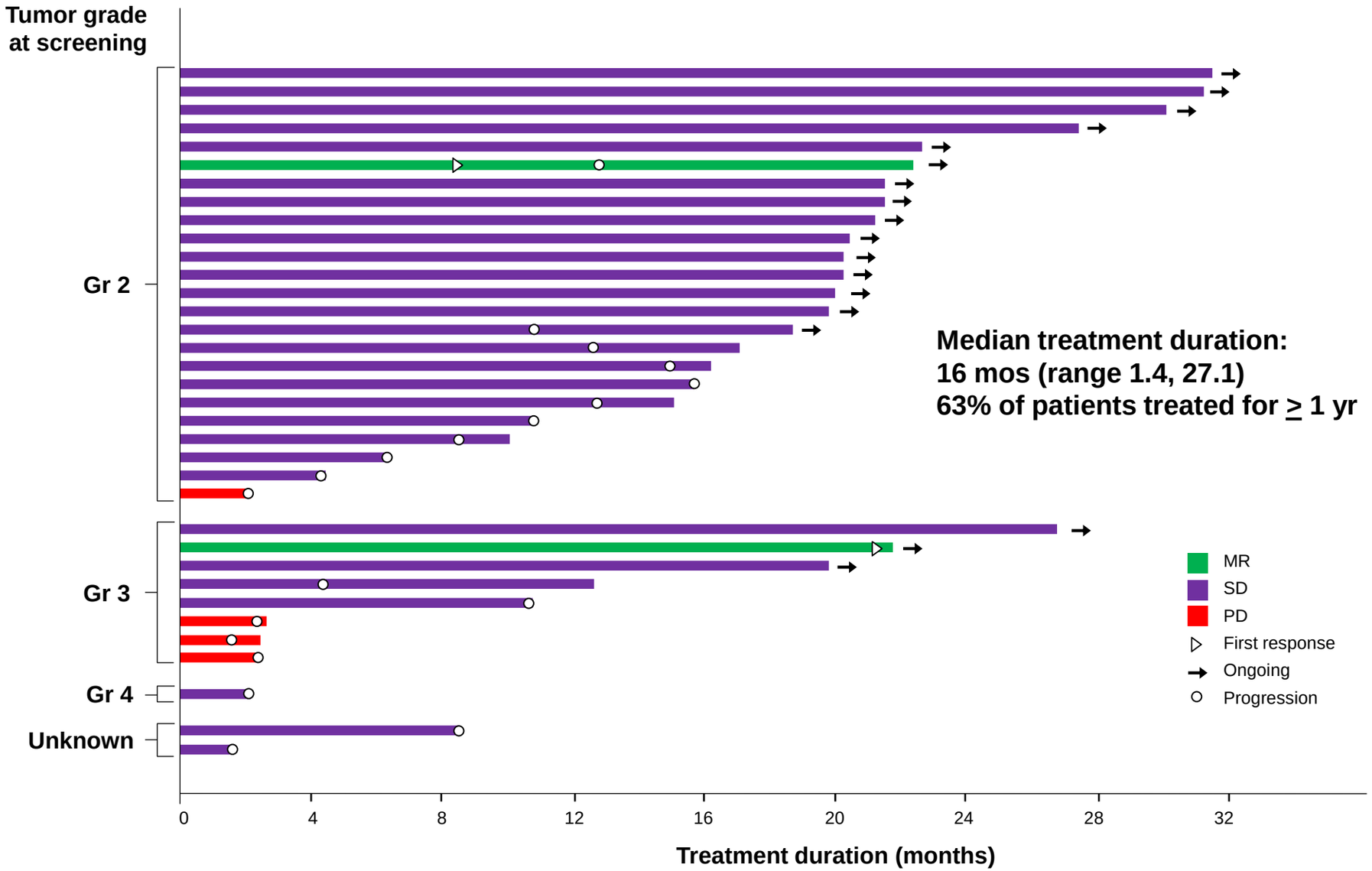
# Low Grade Glioma: High Unmet Need Not Adequately Addressed by Chemotherapy or Radiation




Sources: CDC National Program of Cancer Registries (NPCR); SEER. Cancer Stat Facts; Market research; CBTRUS (Central Brain Tumor Registry in the US); Neurosurg Focus. 2015 Jan; 38(1): E6.

# Durable Stable Disease Signal with Ivosidenib Phase 1 Data

- Ivosidenib well tolerated
- Durable stable disease signal encouraging; 51% of patients still on treatment
- Reduction of tumor growth rates also observed

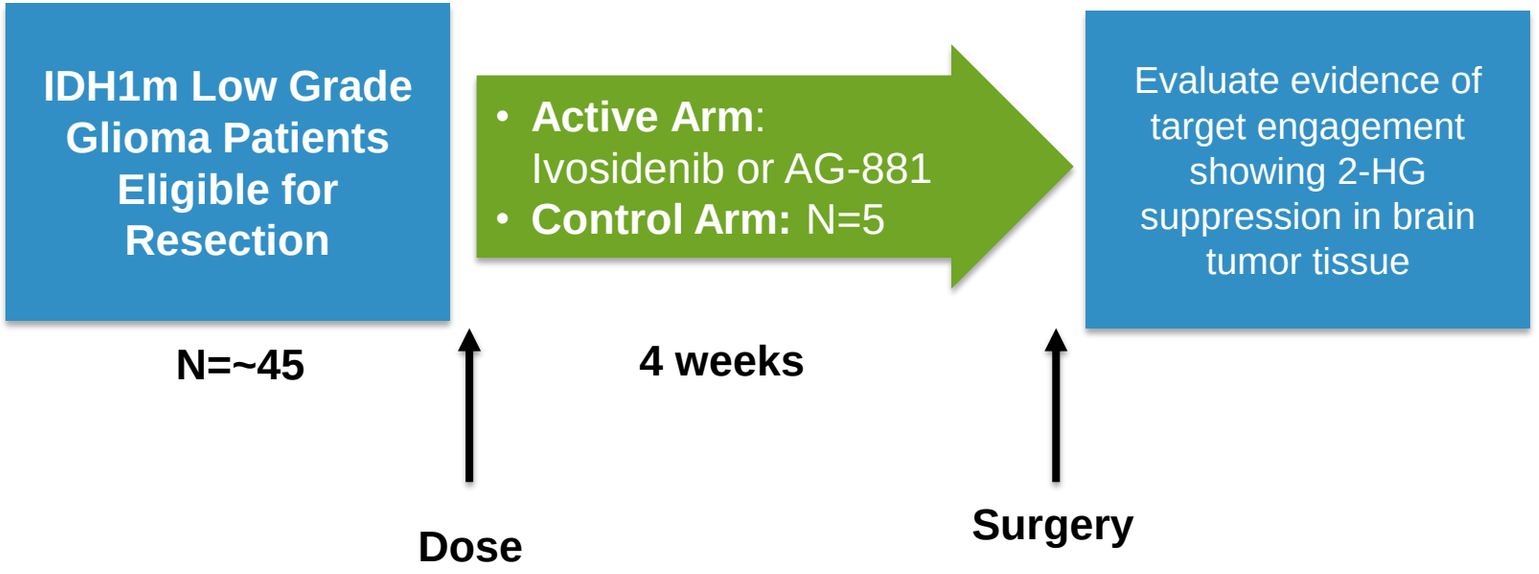



Source: Data presented at SNO 2017

# Ongoing Phase 1 Perioperative Study with Ivosidenib and AG-881 Evaluating Evidence of Target Engagement

## Study Objectives:

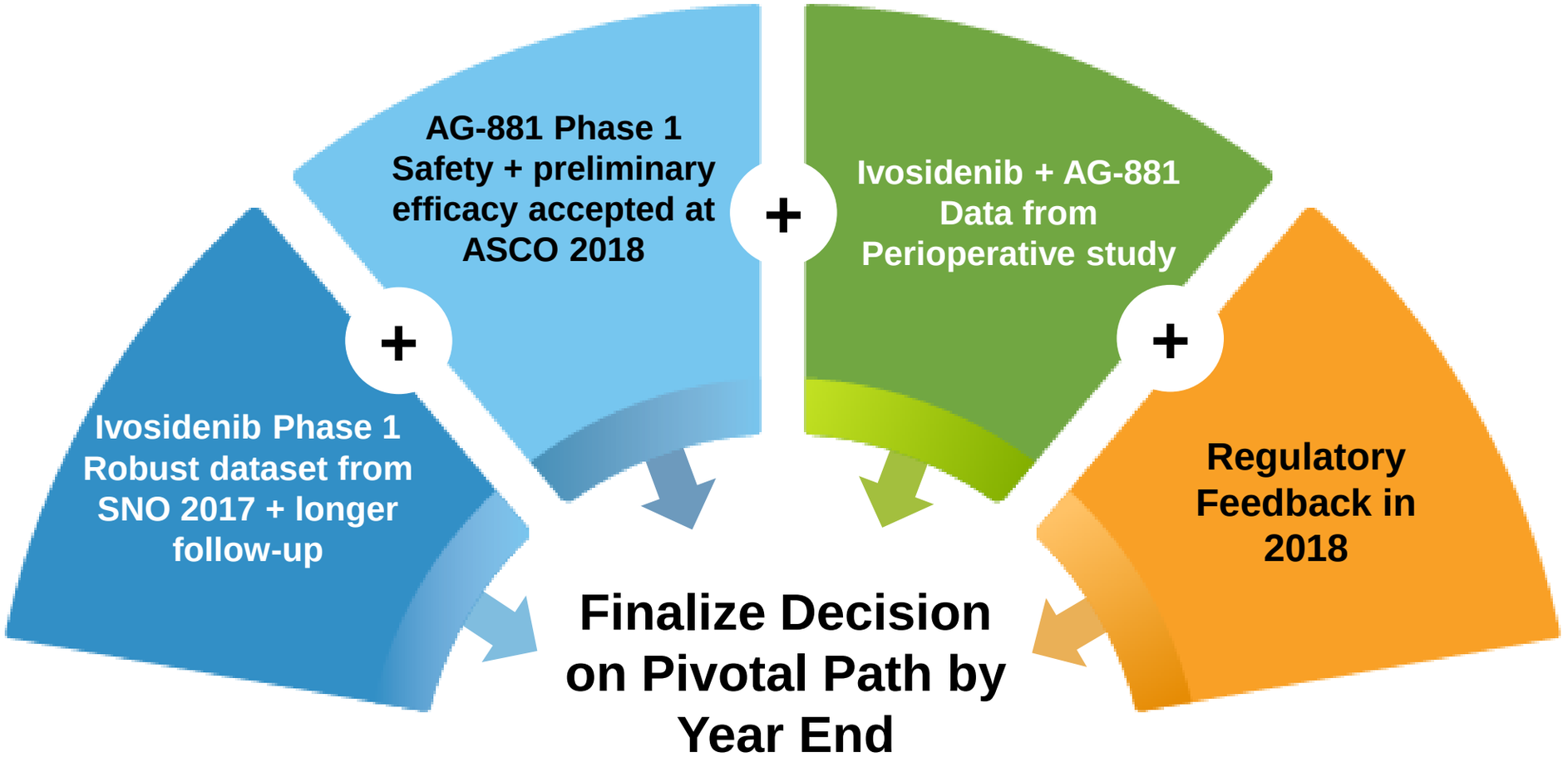
- Determine amount of drug penetration in the brain
- Confirm magnitude of IDHm target engagement as measured by 2HG levels in brain tumor tissue (pre-clincally 85% seen with ivosidenib & 98% with AG-881)
- Assess impact of IDHm inhibition on differentiation and epigenetic profiles in tumor tissue
- Assess the safety of both molecules




ClinicalTrials.gov Identifier: NCT03343197

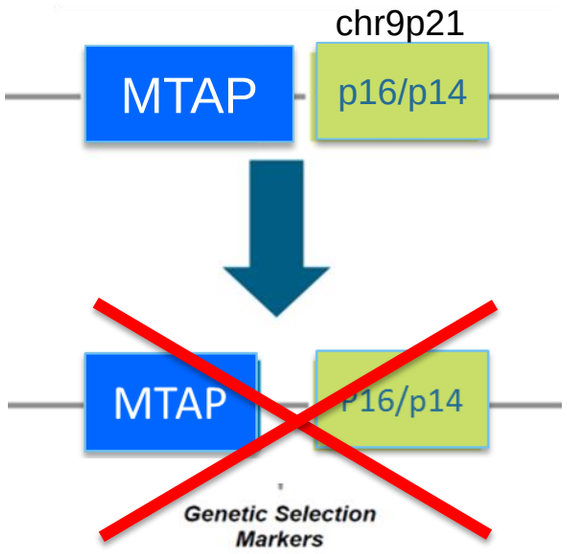
**Trial initiated in Q1; Patients Enrolling**

# Next Steps in Glioma

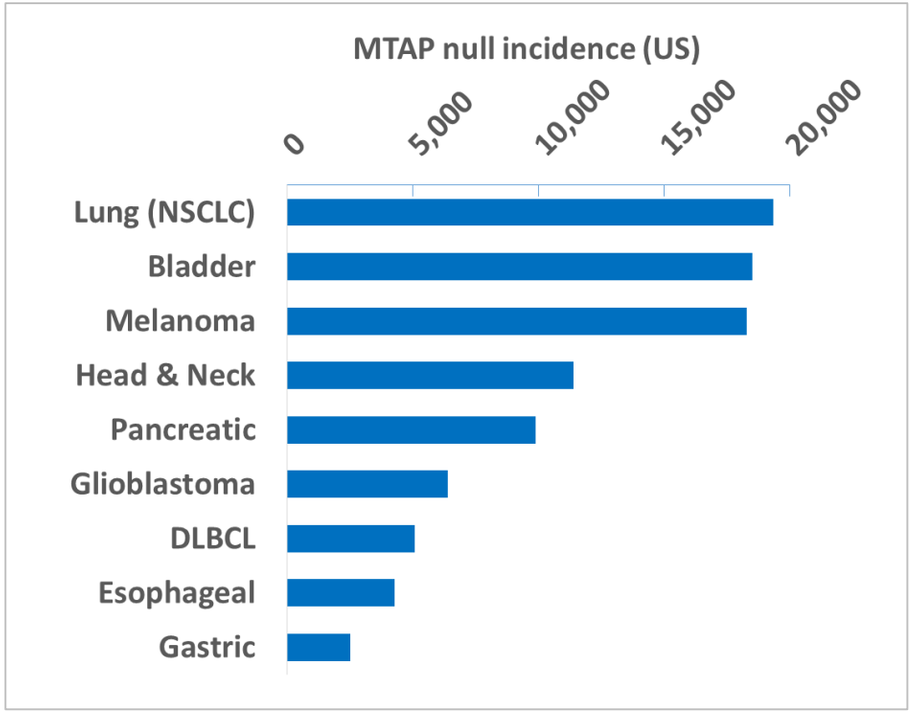


# AG-270 Designed to Target MAT2A in MTAP-Deleted Tumors

**MTAP is the metabolic gene most frequently deleted in cancer because it is adjacent to a common tumor suppressor p16/p14**



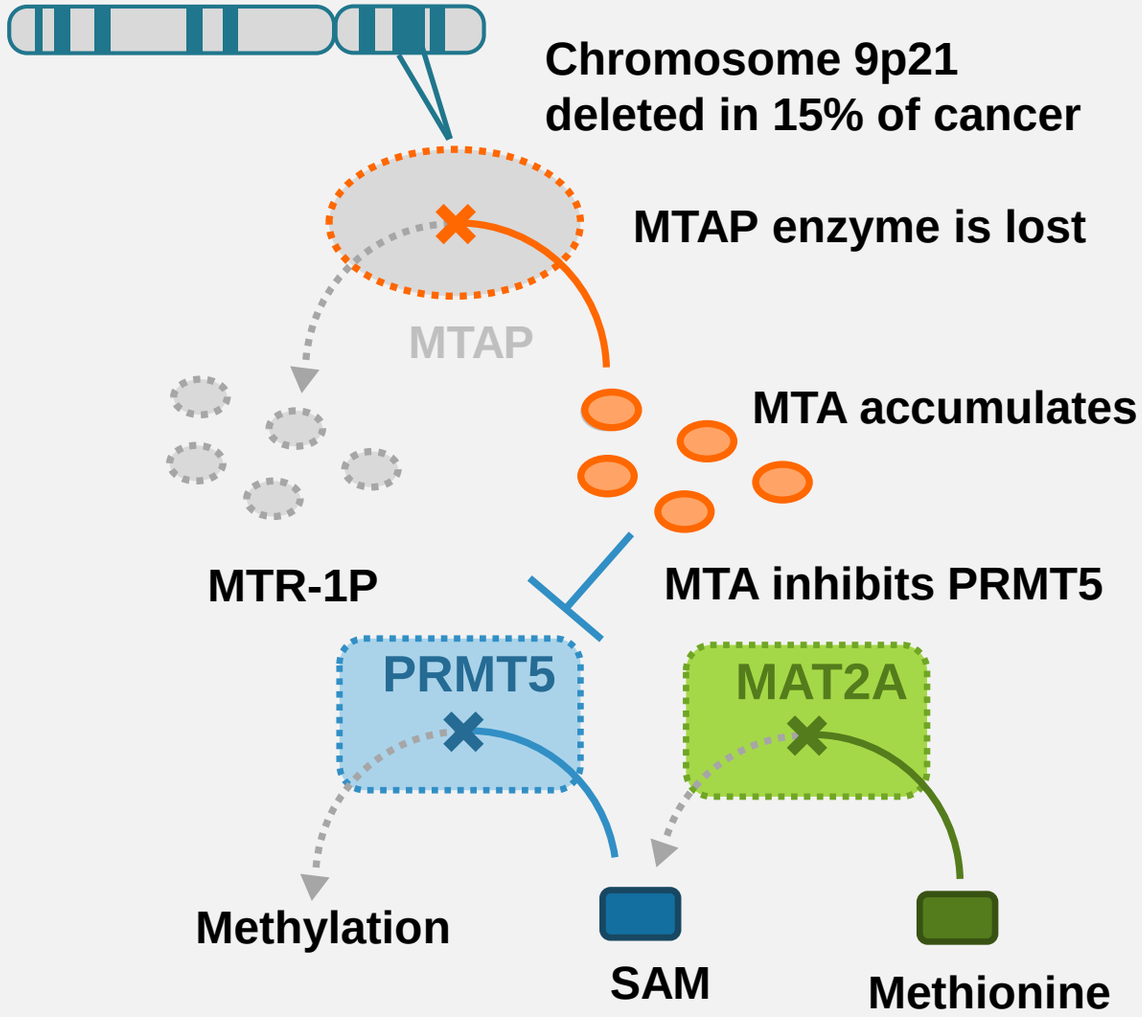

**~98K new patients/year in U.S. with MTAP deletion**




Sources: US Incidence data is from the NCI SEER; MTAP deletion frequencies are from Agios analysis of data from The Cancer Genome Atlas

# A Key Insight: Deletion of MTAP Makes Cancers Vulnerable to Targeting of MAT2A

1. **MTAP deletion**
2. **Substrate MTA accumulates**
3. **Partial inhibition of PRMT5**
4. **Sensitivity to a ‘second hit’: targeting MAT2A starves PRMT5 of its substrate**



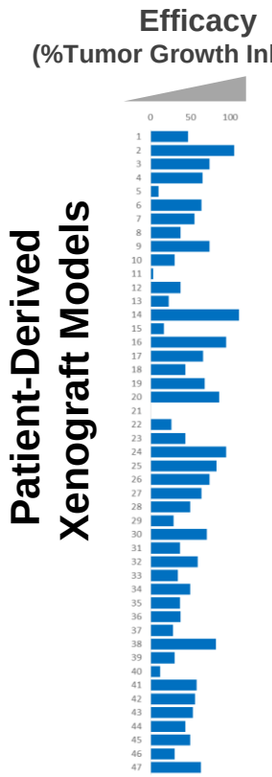


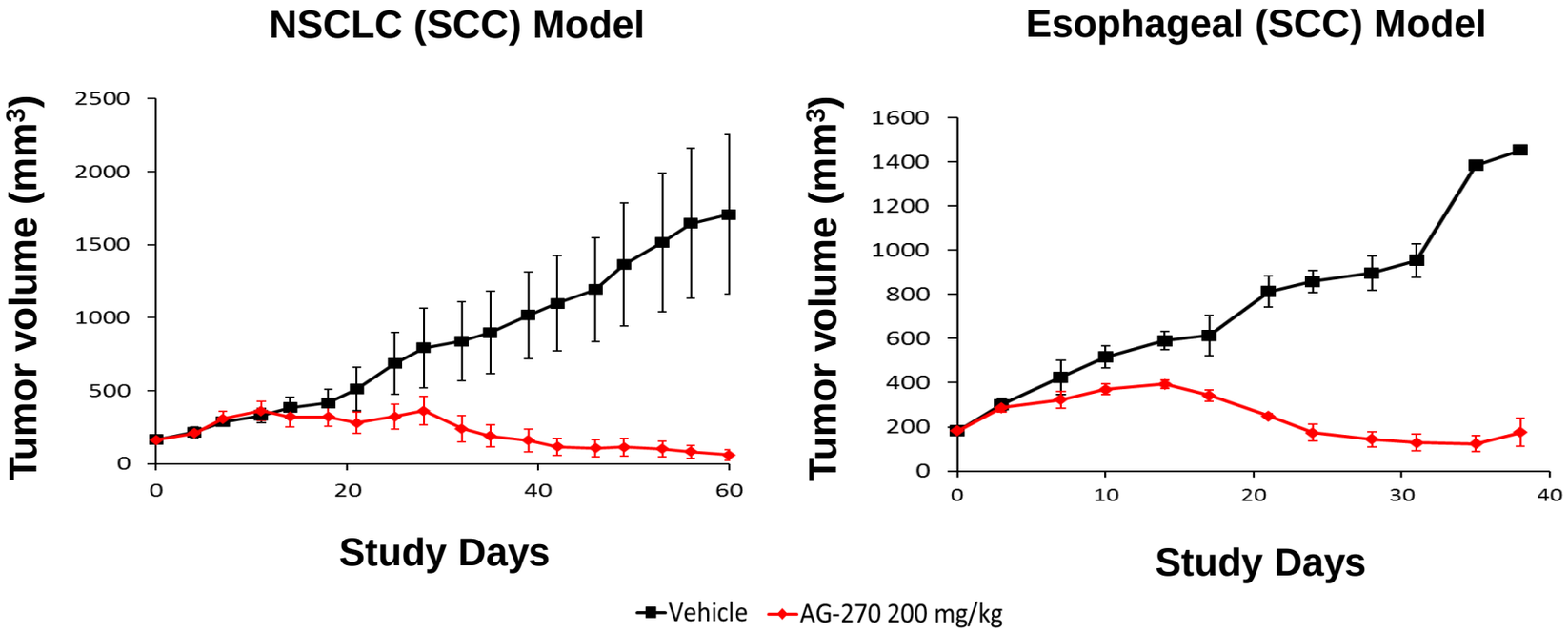

Sources: Marjon et al Cell Reports. 2016 Apr 19;15(3):574-587 and MTAP deletion frequency from Agios analysis of data from The Cancer Genome Atlas

# Preclinical Studies Indicate Potential for Use in Variety of MTAP-Deleted Indications

**Patient-derived Xenograft (PDX) 'clinical trial'**

**Regressions observed upon single agent AG-270 treatment in some models**



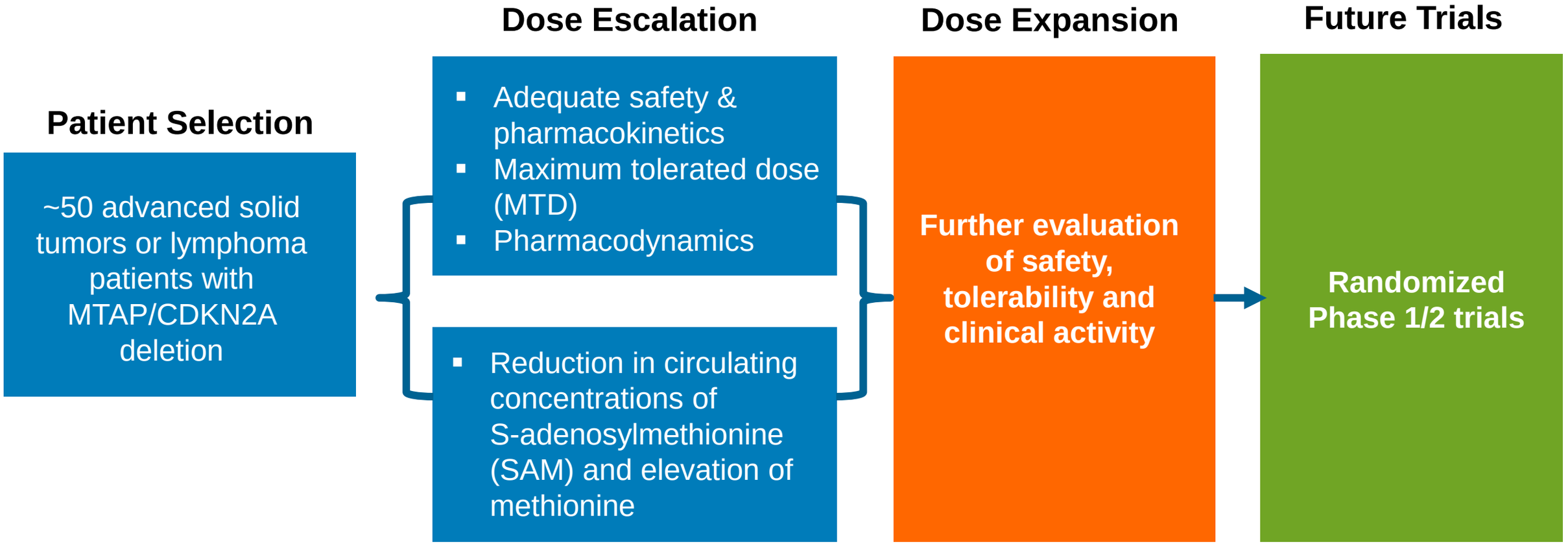




**AG-270 is efficacious in MTAP-deleted PDX models from a variety of tissue origins including NSCLC, pancreatic, gastric & esophageal**



Source: Agios data on file

# AG-270 First-in-Human Phase 1 Clinical Trial




ClinicalTrials.gov Identifier: NCT03435250

**Trial initiated and enrolling patients**

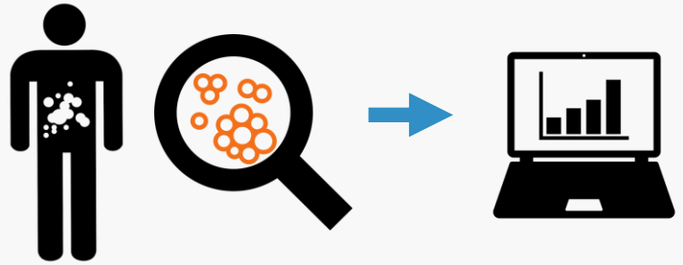
# AG-270 Program Is Well Poised for Biomarker-driven Clinical Development

## Multiple Pharmacodynamic Biomarkers

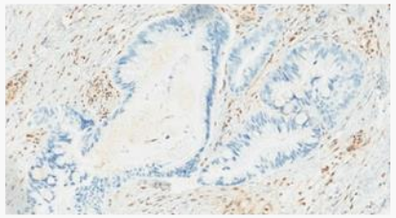
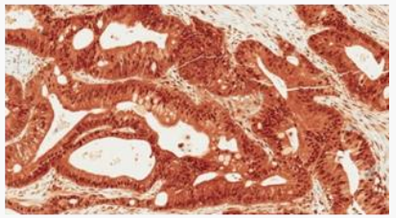
| PATHWAY EFFECTS | CLINICALLY APPLICABLE BIOMARKERS |
|---|---|
| MAT2A inhibition | |
| ↓ Tumor-selective inhibition of PRMT5 | Monitor SAM in patient plasma |
| ↓ Inhibition of PRMT5 targets including the spliceosome | Measure PRMT5 methyl marks in tumor |
| ↓ Antiproliferative & cytotoxic effects | Assess splicing using RNA seq & other assays |

## Patient Selection Biomarkers

**1.** Next-gen sequencing for CDKN2A loss



**2.** Directly assess MTAP-status by IHC

| MTAP deficient PDAC | MTAP positive PDAC |
|---|---|
|  |  |

Source: Agios data on file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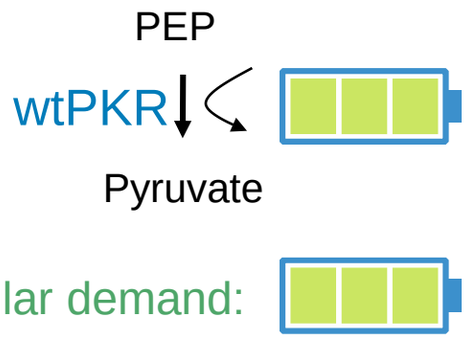
RARE GENETIC DISEASES
RESEARCH

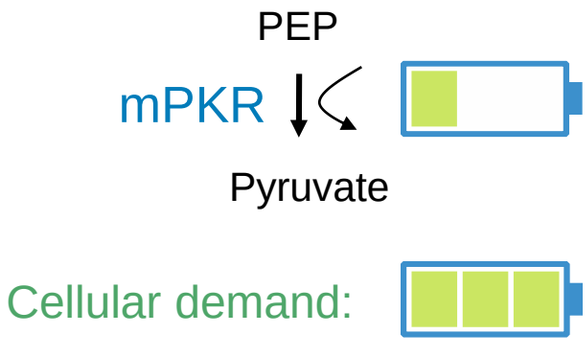
# PK Activation Represents Opportunities Across Hemolytic Anemias

## Normal Red Cell




**ATP production meets demand**

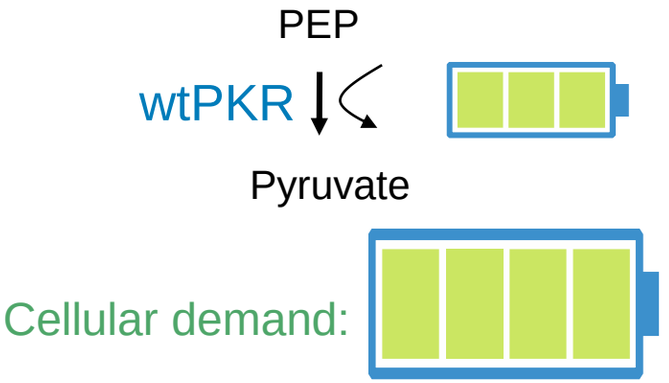
## Pyruvate Kinase Deficiency




**Inadequate production: ATP deficiency**

✓ **Proof of concept achieved**

## Other Hemolytic Anemias

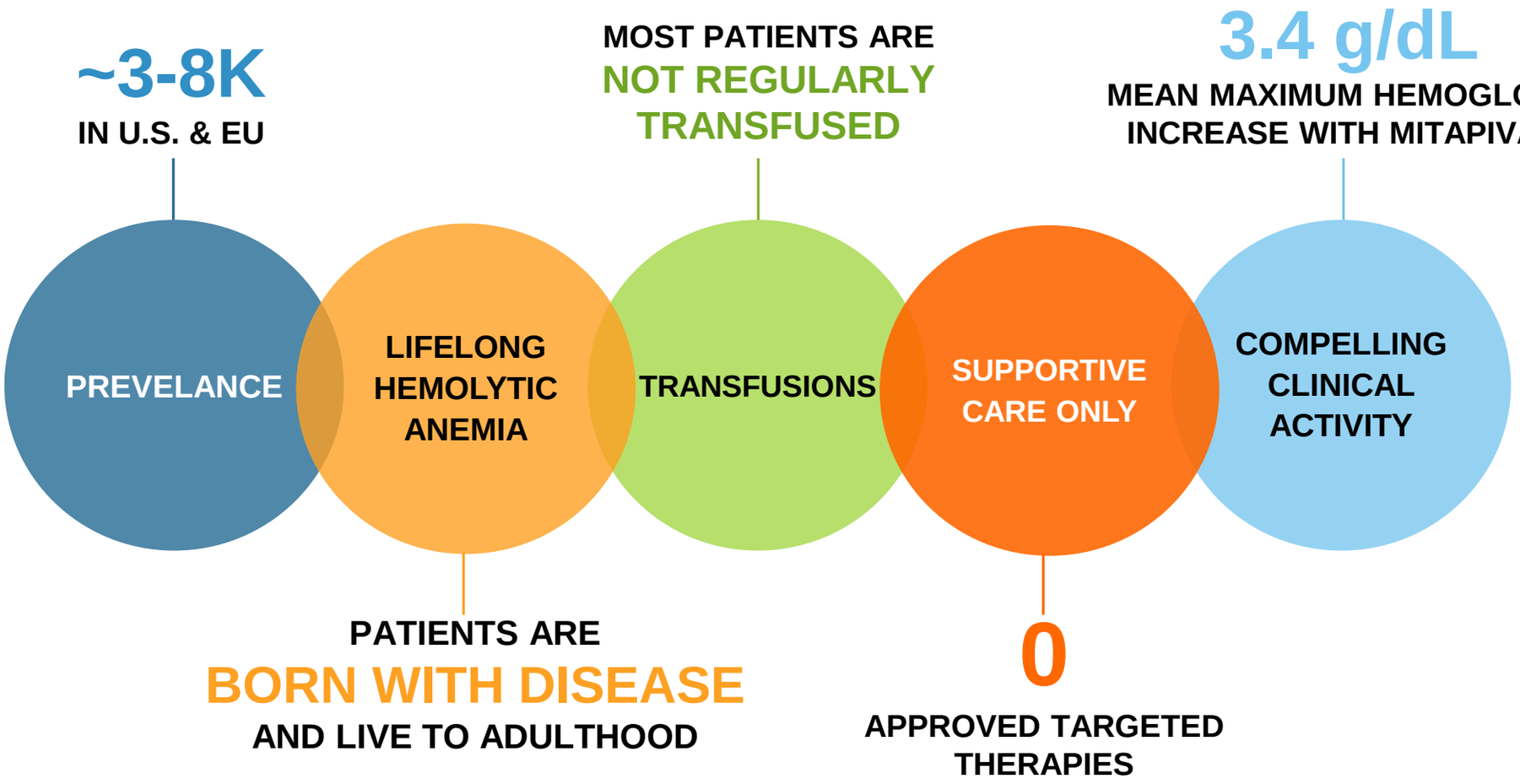



**Increased demand: ATP deficiency**

**Thalassemia:** Expect to initiate Phase 2 proof-of-concept study in Q4 2018

**Sickle cell:** Planning underway

# Opportunity for Mitapivat (AG-348) to be the First Disease-Modifying Treatment for PK Deficiency




Sources: Estimated prevalence range from ~1:20K to ~1:485K 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; data presented at ASH 2017

[1]Mean maximum hemoglobin increase of 3.4 g/dL in patients to had a >1.0 g/dL increase in haemoglobin on study



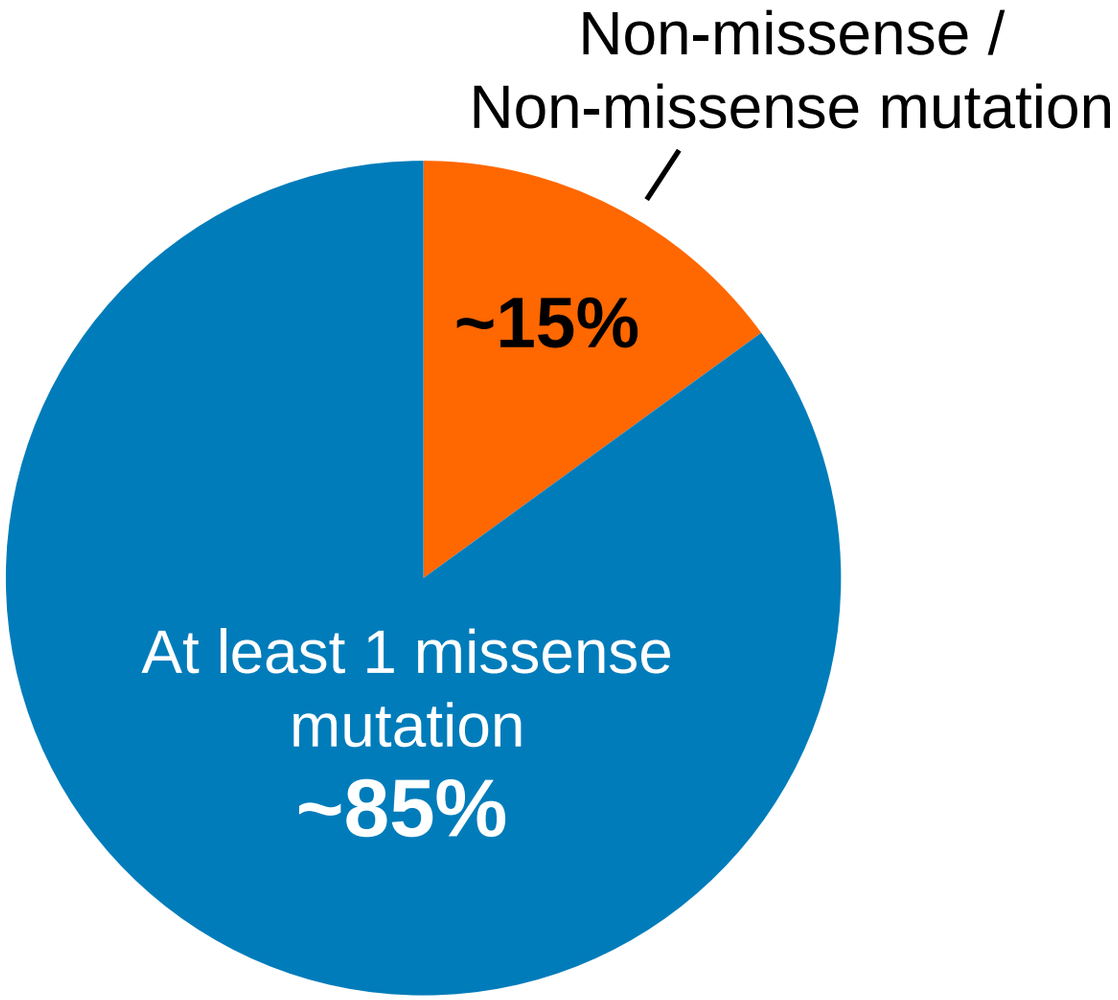
**ACTIVATE and ACTIVATE-T initiated**

# Over 300 Mutations Cause a Range of Defective PKR Proteins

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*

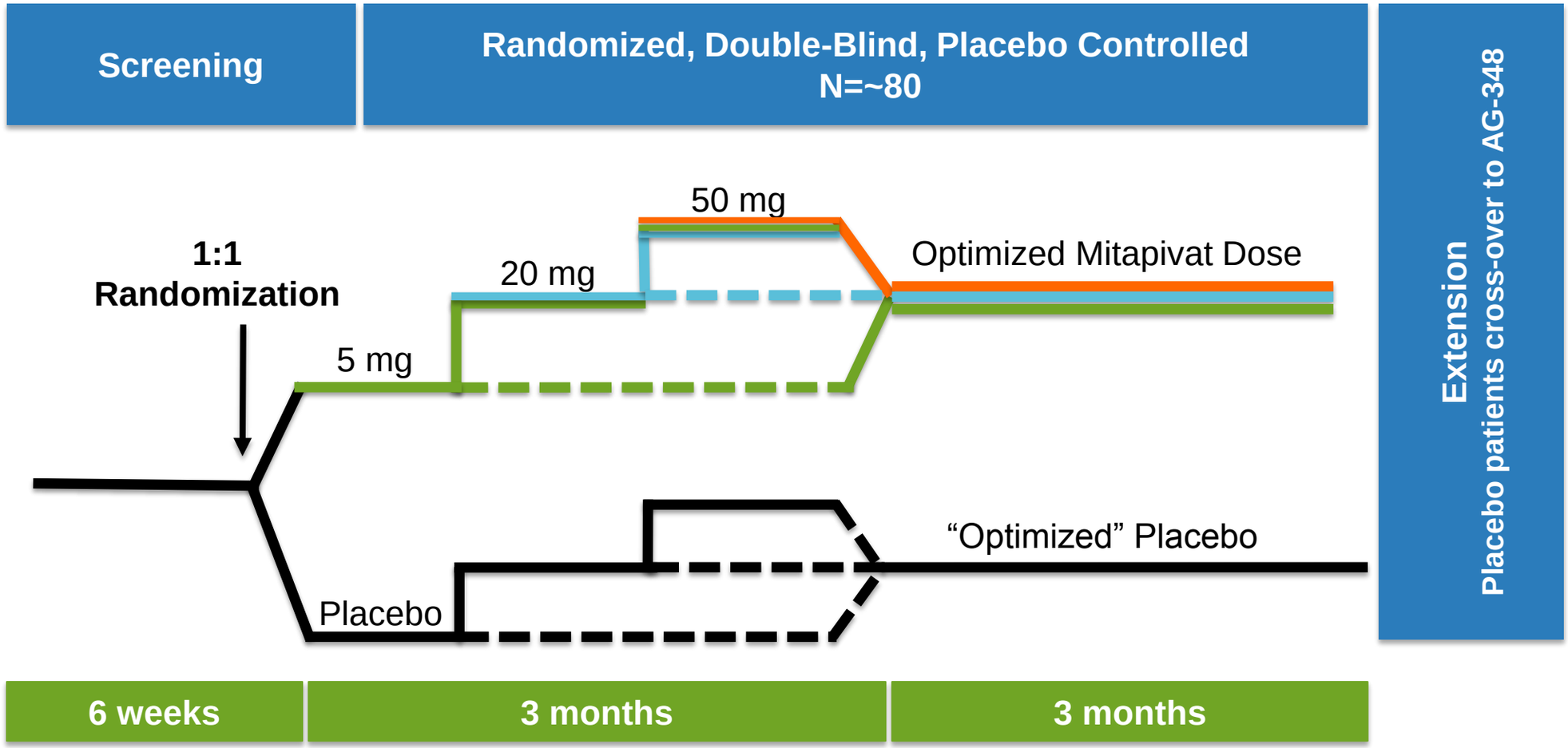
2. **Non-missense mutation** any mutation other than a missense mutation (*e.g.*, stop, frameshift, deletion) – *generally little functional protein*





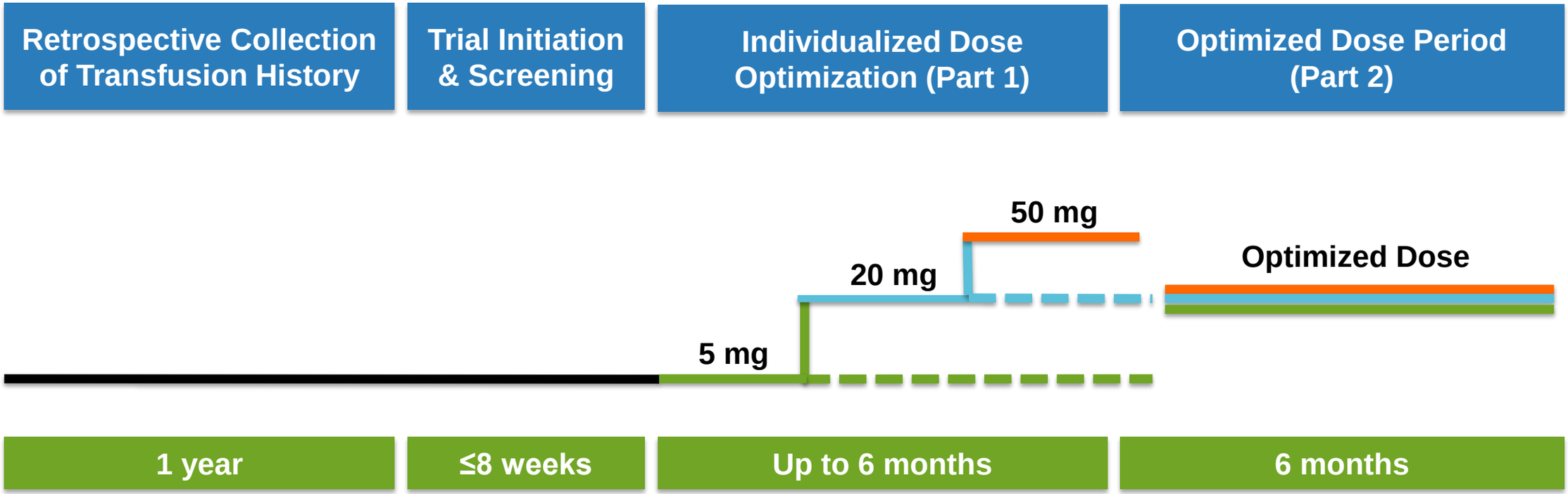

Sources: R van Wijk, Blood 2005; Bianchi P et al. poster, 2017 ASH Annual Meeting

# Mitapivat (AG-348) ACTIVATE Trial for Non-Regularly Transfused Patients




**Primary Efficacy Endpoint:** Proportion of patients who achieve at least a 1.5 g/dL increase in hemoglobin sustained over multiple visits

# Mitapivat (AG-348) ACTIVATE-T Trial for Regularly Transfused Patients

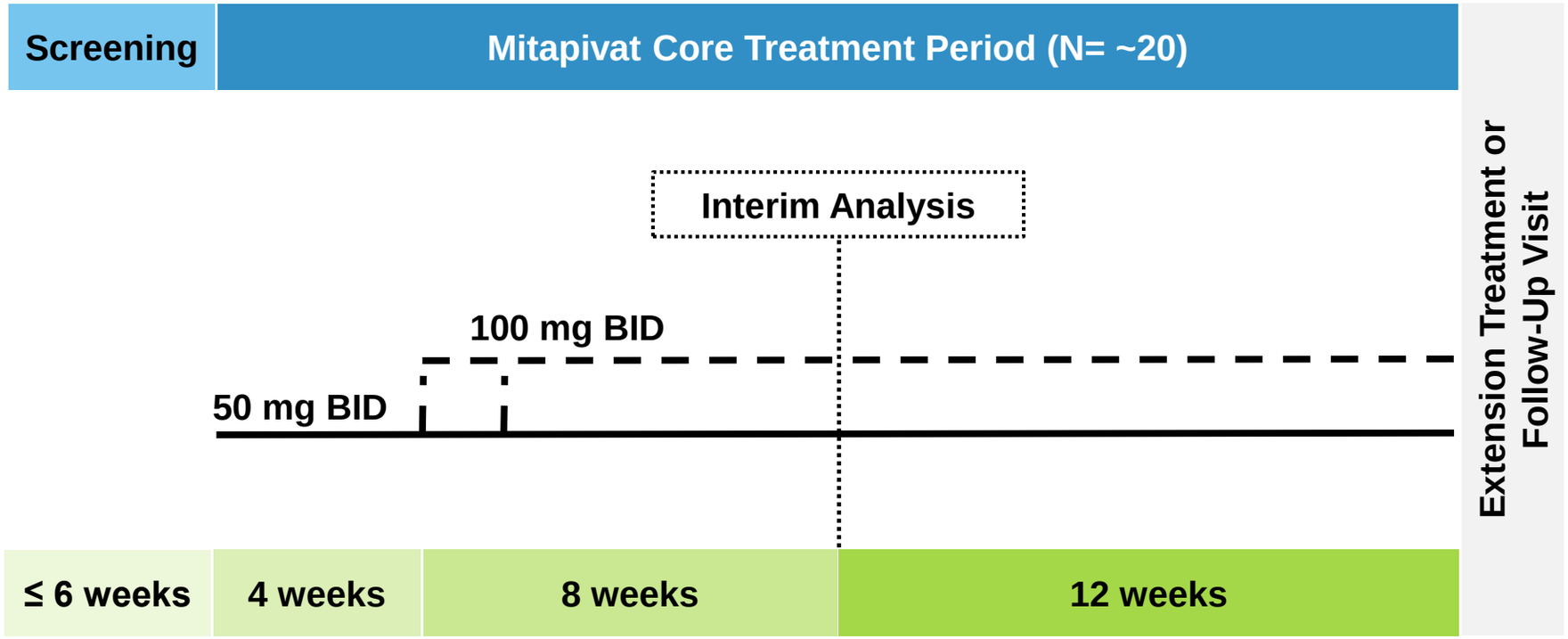



Approximately 20 regularly transfused patients who have required a minimum of 6 transfusions over the year preceding enrollment

**Primary Endpoint:** Reduction in transfusion burden over a 6 month period compared to the patient's transfusion history

# Thalassemia Phase 2 Proof-of-Concept in Non-Transfusion Dependent Adults

- Open-label trial in ~20 patients with hemoglobin < 9.0.
- Primary endpoint is hemoglobin response, using a definition of 1.0 g/dl over baseline at 12 weeks

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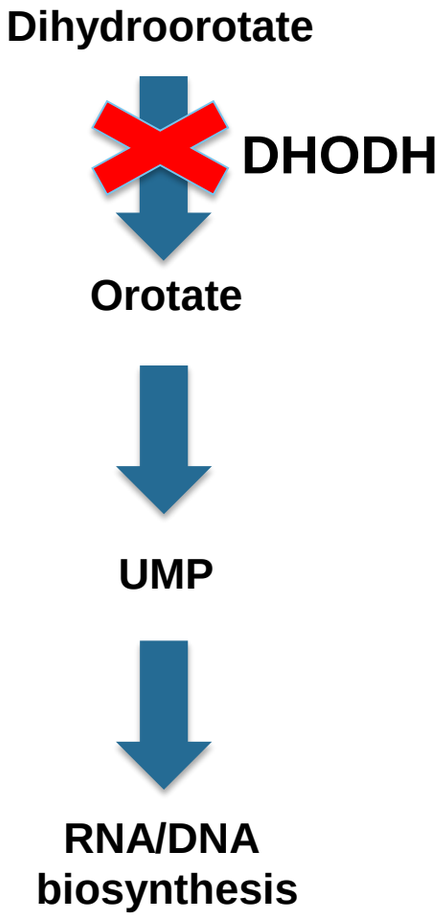
# Agios Preclinical Pipeline

| Program | Target Discovery | Target Validation | Drug Discovery | Drug Candidate |
|---|---|---|---|---|
| **Oncology** | | | | |
| Heme Lineage: AG-636 DHODH | | | | ● |
| MAT2A Follow-Ons | | | ● | |
| PTEN-mutant Solid Tumors | | | ● | |
| Genetically Defined Heme Target | | | ● | |
| Genetically Defined Heme Target | | ● | | |
| Other Exploratory Programs | ◐ | ◐ | | |
| **Rare Genetic Diseases** | | | | |
| Pyruvate Kinase Activator Follow-Ons | | | ● | |
| Phenylketonuria (PKU) | | | ● | |
| Erythroid Porphyria | | | ● | |
| Friedreich's Ataxia | | | ● | |
| Other Exploratory Programs | ◐ | ◐ | | |
| **Metabolic Immuno-Oncology (Celgene Collaboration)** | | | | |
| T-cell and Tumor Target | | | ● | |
| Macrophage Target | | | ● | |
| Macrophage Target | | ● | | |
| Tumor Target | | ● | | |
| Other Targets (T-cell, Macrophage, Tumor) | ● | ● | | |

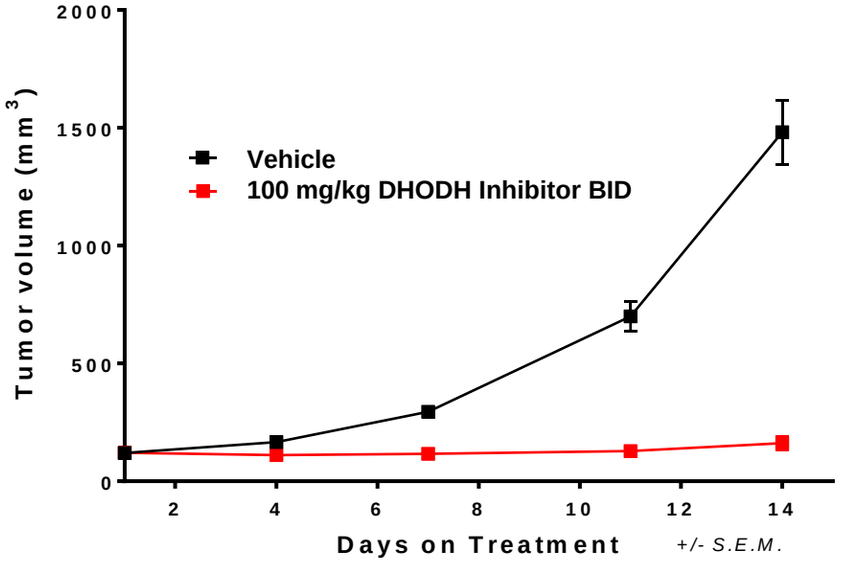
● Metabolic Target ● Non-Metabolic Target ◐ Metabolic and Non-Metabolic Targets ▬ Celgene Collaboration

# DHODH Inhibitor Program IND Expected in Q4 2018

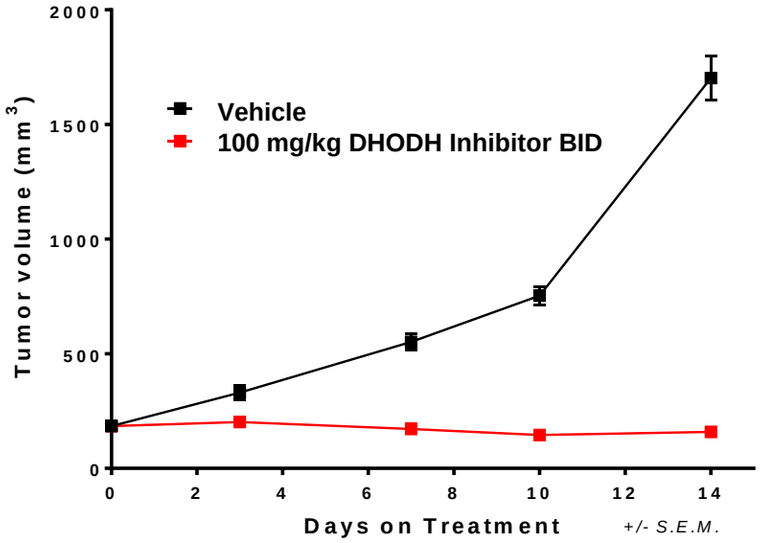
**DHODH catalyzes a critical step in pyrimidine biosynthesis**




Efficacy in MOLM13 **AML** model




Efficacy in OCILY19 **DLBCL** model

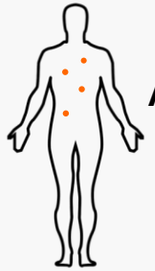



- Agios discovered a lineage-specific dependence on dihydrooroate dehydrogenase (DHODH) in hematologic malignancies (particularly AML and DLBCL)
- DHODH Inhibition is anticipated to differentiate from standard of care therapies
  - Activity in cancers that are resistant to standard-of-care chemotherapeutics
  - Mechanism of antitumor effect a combination of cell growth arrest and cellular differentiation

Sources: Sykes et al Cell 2016, Agios data on file

# Phenylketonuria (PKU): Mutations in Phenylalanine Hydroxylase (PAH)

**1. Normal Protein Diet**

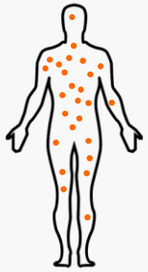


A mixed diet provides your body Phe

**2. Defective PAH enzyme**

PAH fails to process the Phe to Tyr


**3. Increase in Phenylalanine**



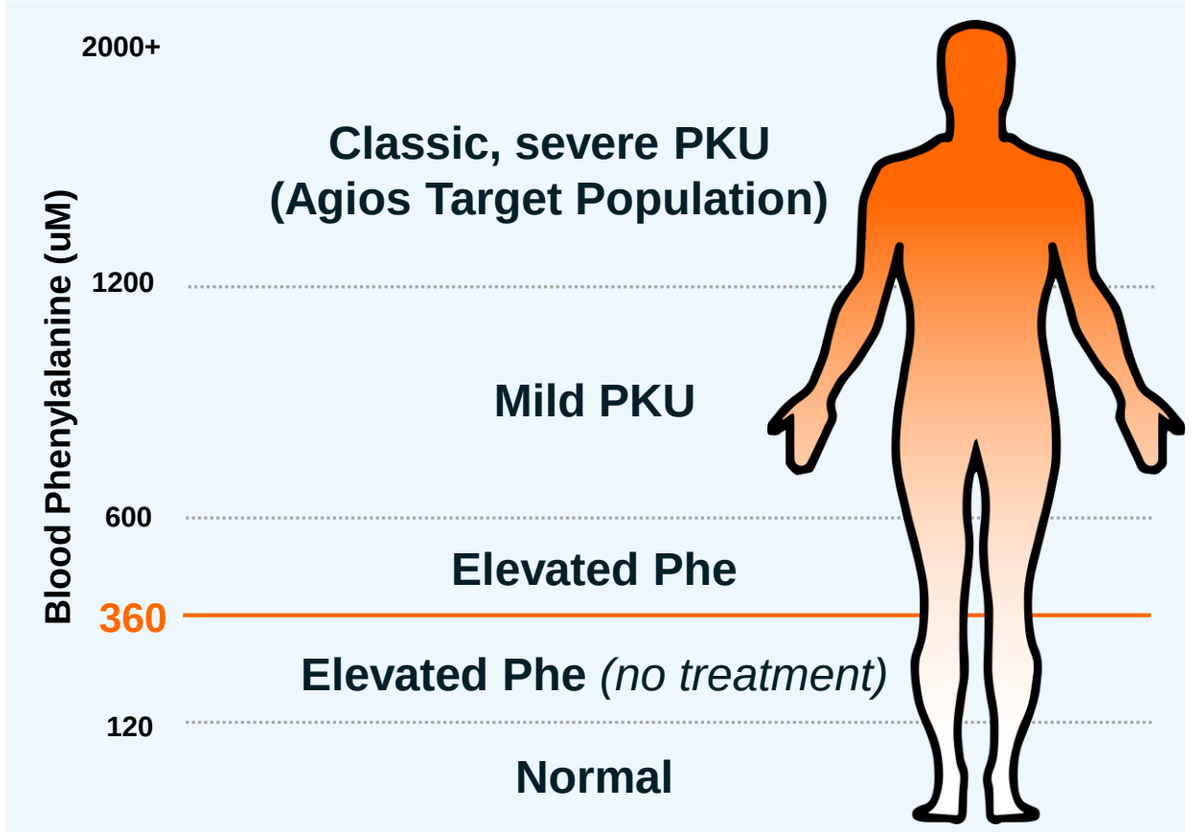
This leads to high Phe levels in the blood which results in neurocognitive defects

- ~16,000 PKU patients in U.S.
- ~60% of patients have severe disease
- Severity of disease correlates with extent of phenylalanine elevation
- Phenylalanine elevation causes neurocognitive defects, demyelination and intellectual disability
- High unmet medical need remains:
  - Highly restricted diet is key part of SOC
  - No effective approved treatment for severe patients

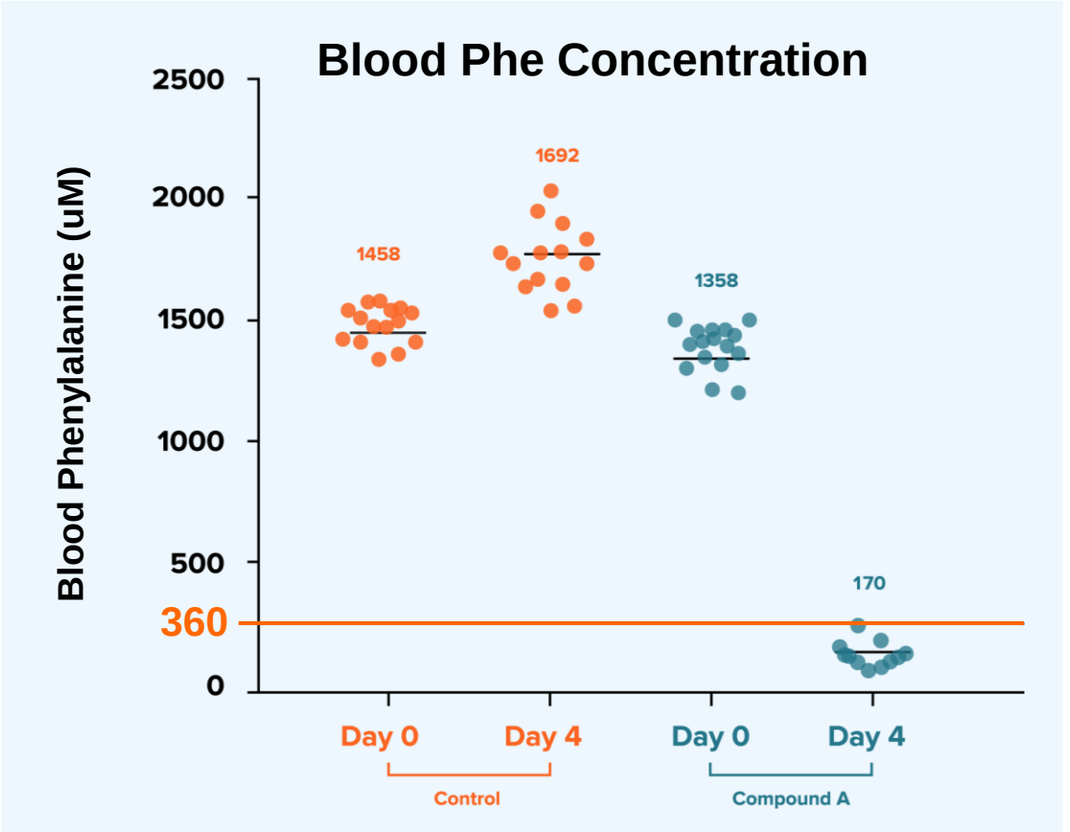


Sources: National PKU Alliance, www.npkua.org and Weisbren et al ‘Phenylalanine blood levels and clinical outcomes in phenylketonuria’

# Agios Lead Molecule Dramatically Decreases Blood Phenylalanine Levels in Severe PKU Mouse Model




**Severity of disease correlates with extent of phenylalanine elevation** Phe




**Blood Phe concentrations of treated mice normalized**

Source: Agios data on file

# CORPORATE

# Second Quarter 2018 Financial Results

| Balance Sheet | June 30, 2018 | December 31, 2017 | Variance |
|---|---|---|---|
| Cash, Cash Equivalents and Marketable Securities | $937M | $568M | $369M |
| Total Assets | $998M | $614M | $384M |

| Statement of Operations | Three Months Ended June 30, 2018 | Three Months Ended June 30, 2017 | Variance |
|---|---|---|---|
| Collaboration Revenue | $38.8M | $11.3M | $27.5M |
| Royalty Revenue | $1.6M | -- | $1.6M |
| Research & Development Expense (1) | $86.7M | $79.8M | $6.9M |
| General & Administrative Expense | $26.6M | $16.1M | $10.5M |

*1) The R&D expenses reported for the three months ended June 30, 2017 are reported net of cost reimbursements of $2.5 million, for the three months ended June 30, 2018 cost reimbursements are reflected in Collaboration Revenue.*

**June 30, 2018 cash balance provides runway through at least the end of 2020**

# 2018 Goals Set Stage for Building Long-Term Value

## 2018 GOALS

- ✓ Secure approval and commercialize TIBSOVO® for R/R AML in the U.S.
- Initiate Phase 3 frontline AML trial combining ivosidenib & enasidenib with 7+3
- ✓ Initiate mitapivat PK deficiency pivotal trials
- ✓ Initiate AG-270 Phase 1 dose-escalation trial
- Submit ivosidenib European MAA
- ✓ Initiate glioma perioperative study
- Initiate mitapivat Phase 2 trial in thalassemia
- Submit 7th IND for DHODH

**Vision for 2018 & Beyond**

- At least 3 approved medicines
- Multibillion dollar commercial opportunity across clinical portfolio
- Research engine primed to potentially deliver multiple INDs over next 24 months