Agios Pharmaceuticals

37th Annual J.P. Morgan Healthcare Conference

January 7, 2019

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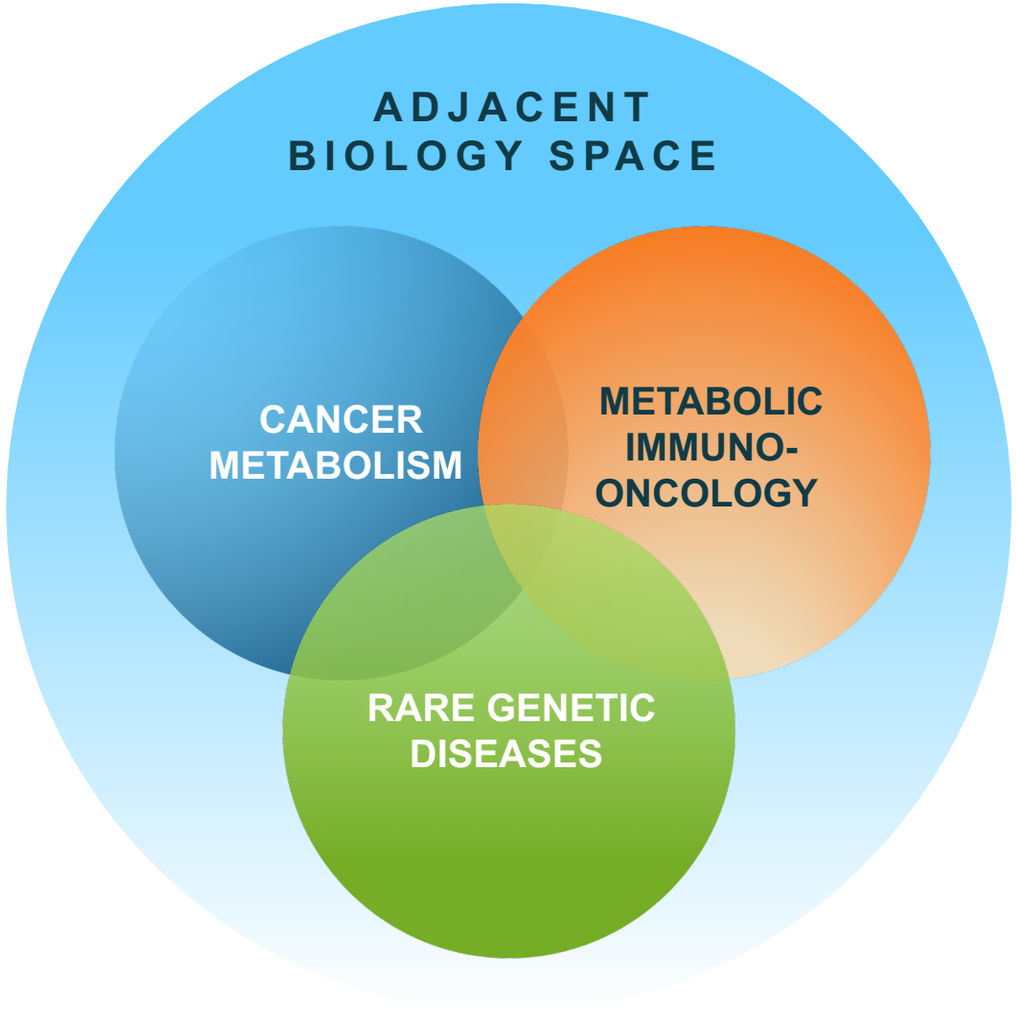
Chief Executive Officer, Agios

Forward Looking Statements

This presentation and various remarks we make during this presentation contain forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Agios' plans, strategies and expectations for its and its collaborator's preclinical, clinical and commercial advancement of its drug development programs including TIBSOVO® (ivosidenib), IDHIFA® (enasidenib), vorasidenib (AG-881), mitapivat, AG-270 and AG-636; the potential benefits of Agios' product candidates; its key milestones for 2019; its estimates regarding its balance of cash, cash equivalents and marketable securities for the year ended December 31, 2018; 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," "expect," "hope," "milestone," "plan," "potential," "possible," "strategy," "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 collaborators is developing will successfully commence or complete necessary preclinical and clinical development phases, or that development of any of Agios' product candidates will successfully continue. There can be no guarantee that any positive developments in Agios' business will result in stock price appreciation. Management's expectations and, therefore, any forward-looking statements in this presentation and various remarks we make during this presentation could also be affected by risks and uncertainties relating to a number of other important factors, including: Agios' results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA, the EMA or other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; Agios' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials; unplanned cash requirements and expenditures; competitive factors; Agios' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; Agios' ability to maintain key collaborations, 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.

Executing Against Our Vision and Values

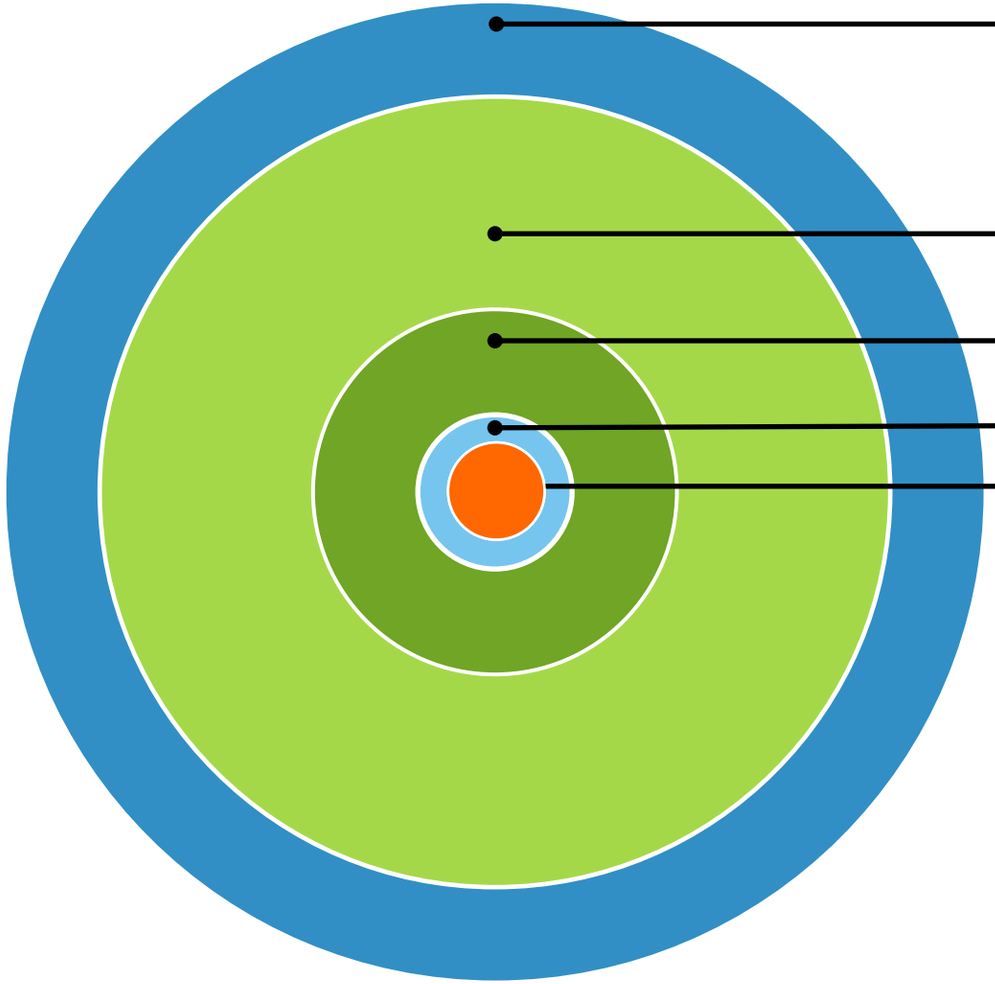
Driven By a Clear Vision and Values



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 One of the Next Great Pharmaceutical Companies



Biotech startups

Agios founded in 2008;
labs opened in Jan. 2009

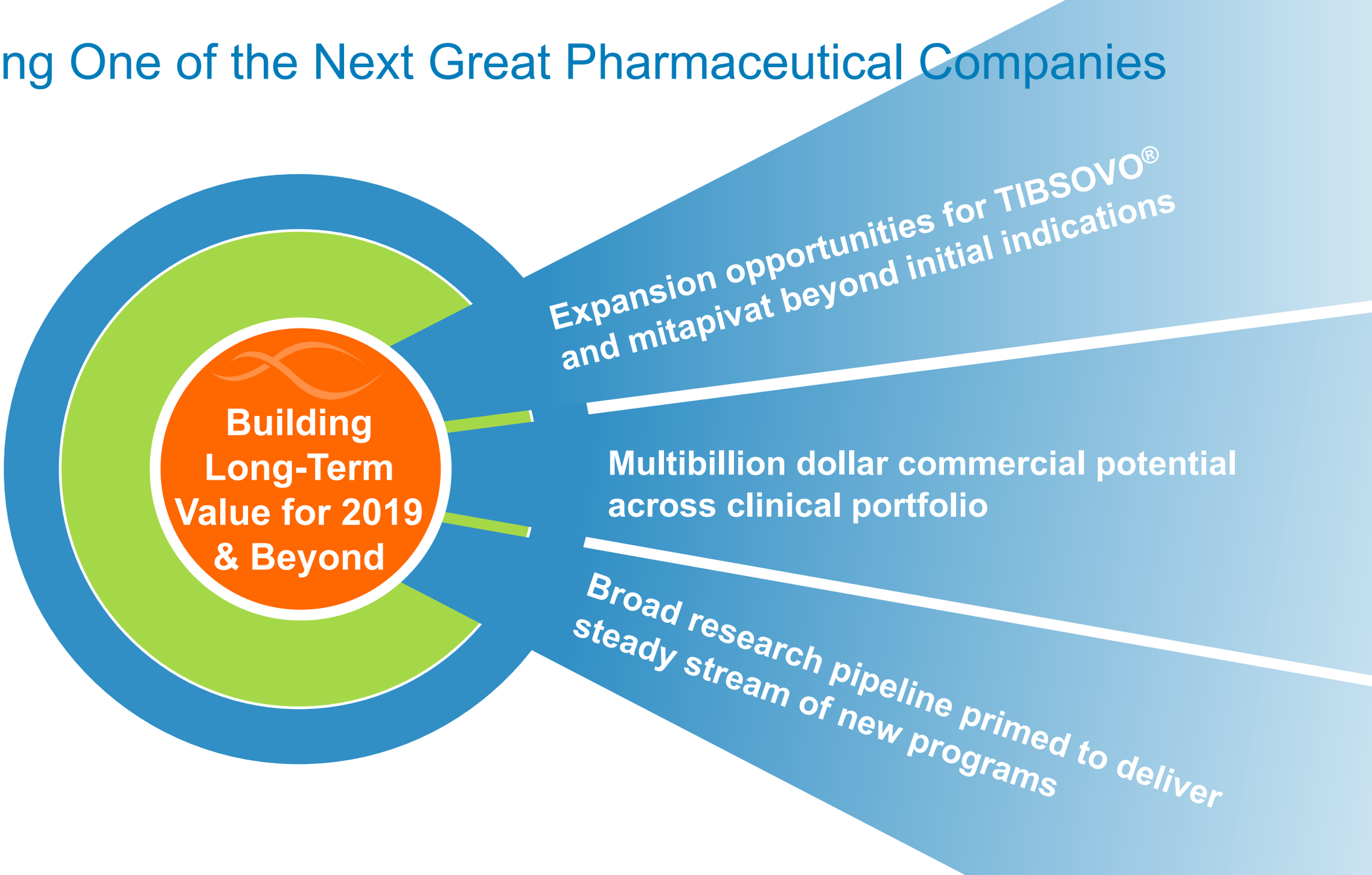
Initiated clinical trials

One drug approved

Two drugs approved

Sustainable multiproduct companies

Building One of the Next Great Pharmaceutical Companies



Agios' Scientific Platform Demonstrates Remarkable, Reproducible Productivity

DISCOVERY

$50-60M
INVESTED IN DRUG DISCOVERY ANNUALLY

7 INDs

SCIENCE

50+
PEER-REVIEWED PUBLICATIONS

15+ ACTIVE RESEARCH PROGRAMS

1,000+
PATIENTS TREATED IN CLINICAL TRIALS

CULTURE

475+ EMPLOYEES

1 VISION

6 DISEASES

5 PIVOTAL CLINICAL TRIALS

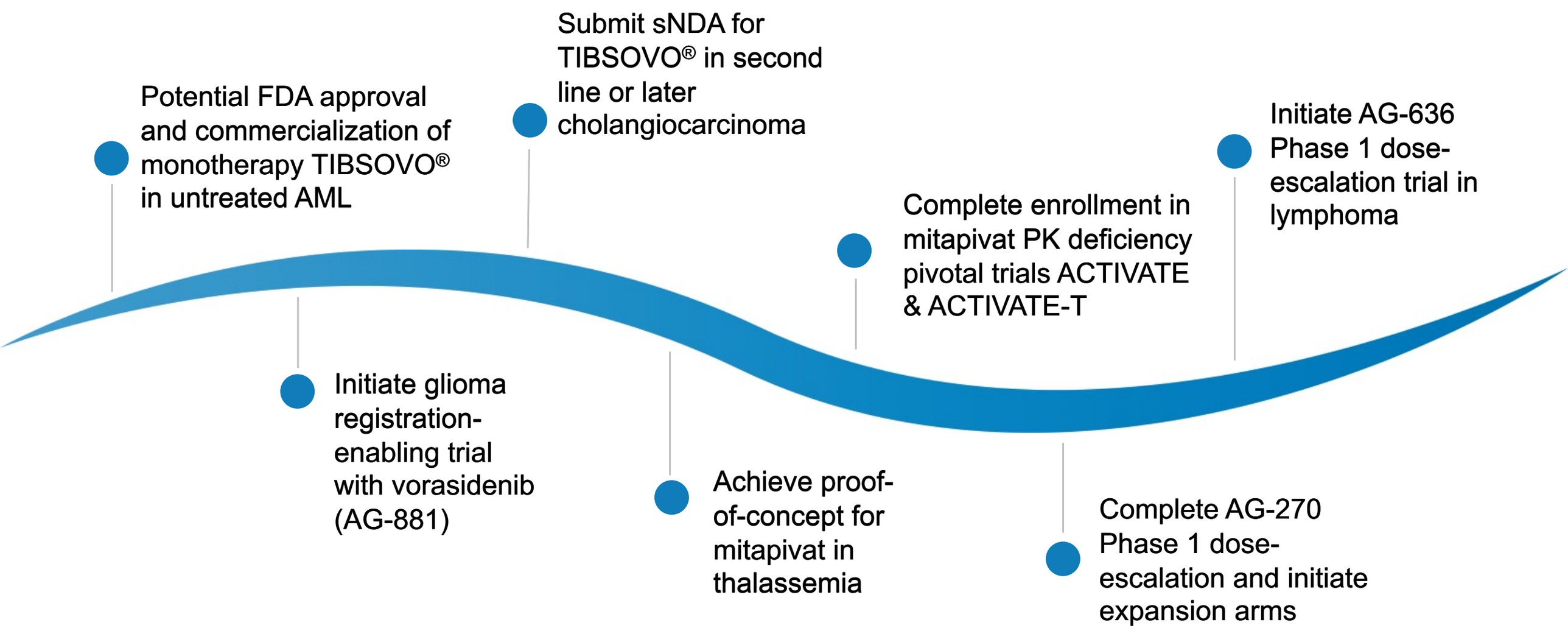
8 ADDITIONAL CLINICAL TRIALS

2 MEDICINES APPROVED

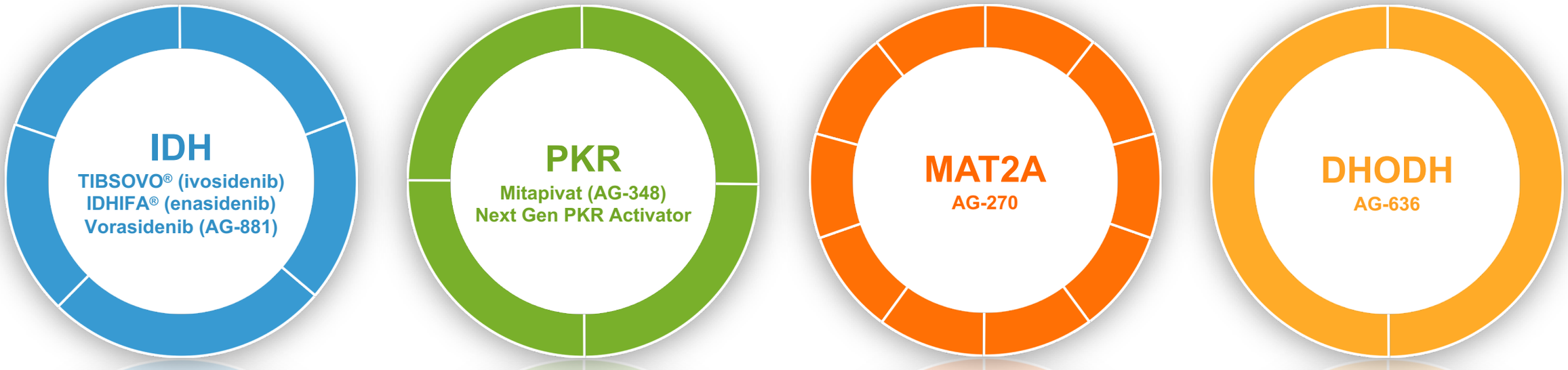
+

4 ADDITIONAL COMPOUNDS IN CLINICAL DEVELOPMENT

2019 Key Milestones Position Agios for Long-term Value Creation



Productive Research & Discovery Engine Has Produced Four Key Targets with Multiple Disease Opportunities



AML
Low Grade Glioma
Cholangiocarcinoma
Chondrosarcoma
MDS

Adult PK Deficiency
Pediatric PK Deficiency
Sickle Cell Disease
Thalassemia

NSCLC
Bladder
Melanoma
Head & Neck
Pancreatic
Glioblastoma
DLBCL
Esophageal
Gastric
Mesothelioma

Lymphoma
AML

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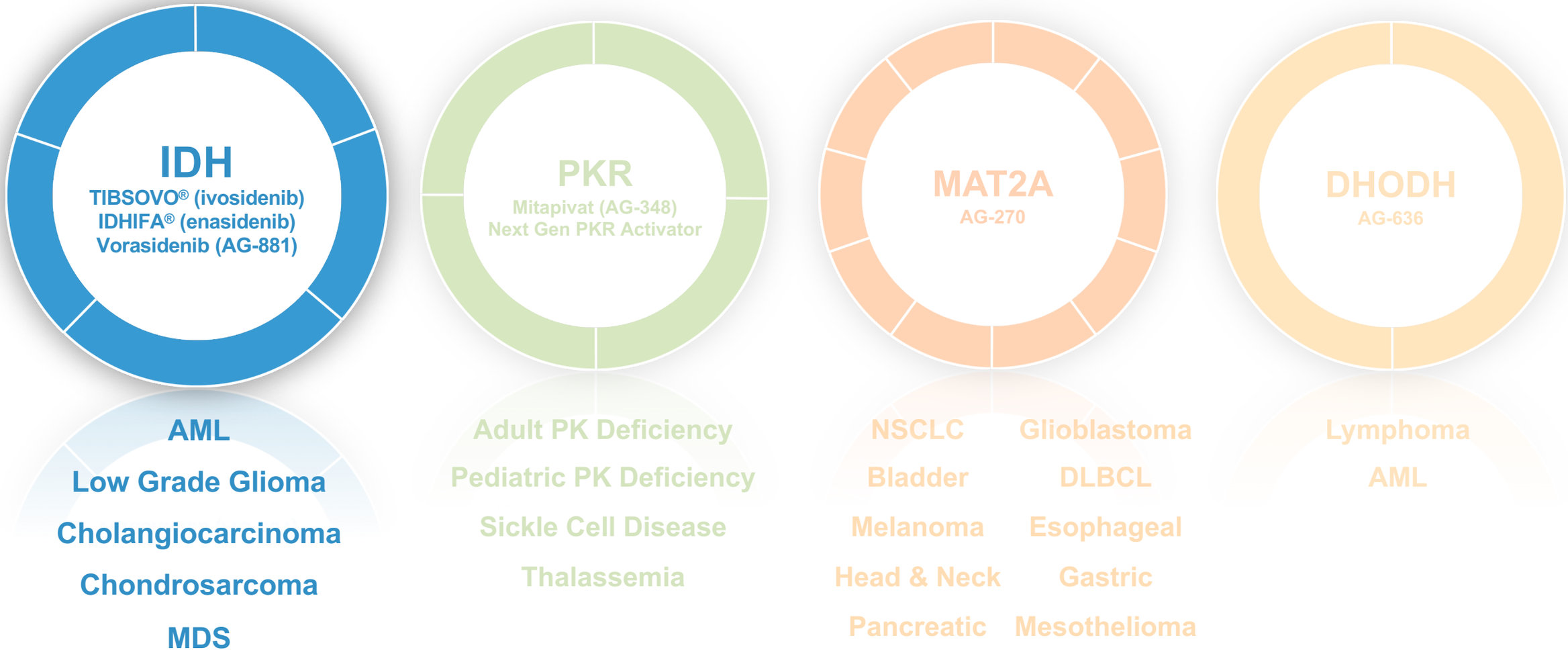


What's Possible for IDHm Patients

NOW

- Relapsed/Refractory AML

NEXT

- Newly diagnosed AML ineligible for standard treatment
- 2L Cholangiocarcinoma

FUTURE

- Low Grade Glioma
- IC-eligible frontline AML
- IC-ineligible frontline AML
- MDS
- Chondrosarcoma

Strong Launch in the Relapsed/Refractory Population Sets the Stage for IDHm Inhibitors as the Cornerstone of AML Therapy

~50K U.S. and EU Annual Newly Diagnosed AML Patients

IDH1/2m is ~20%

RELAPSED / REFRACTORY
~50% of Treated Patients

IDHIFA® (enasidenib) tablets
100mg • 50mg

U.S. Co-commercialization with Celgene

TIBSOVO® (ivosidenib) tablets

MAA
Submitted in Dec. 2018

~80%
Physicians Testing for IDH1/IDH2 mutations*

~200
Total Unique Prescribers as of Q4 2018*

+100%
Increase From Q3 2018

 Sources: Market research as of Dec. 2018; Agios estimates; SEER. Cancer Stat Facts: AML 2015 and Epiphany EPIC oncology numbers; American Cancer Society. AML 2017.; *U.S. only

Shifting the Treatment Paradigm for Patients with Newly Diagnosed IDH1m AML

~50K U.S. and EU Annual Newly Diagnosed AML Patients

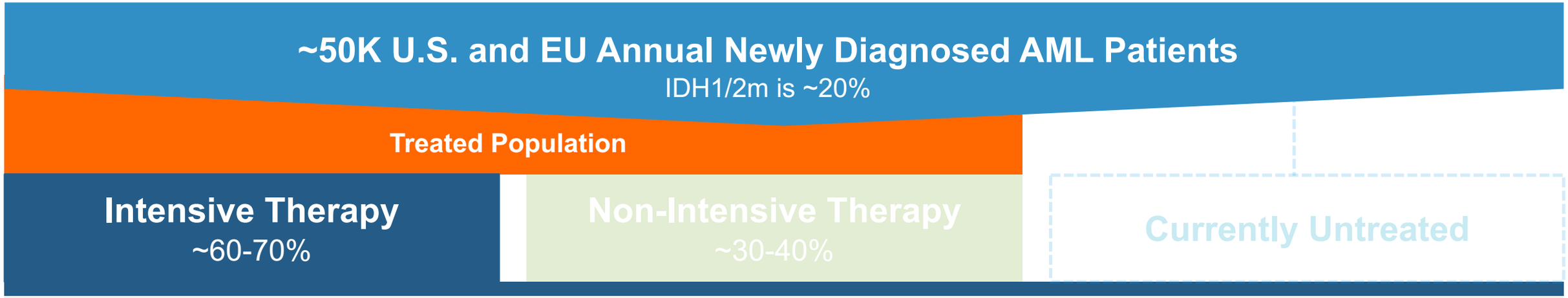
IDH1/2m is ~20%

Treated Population

Intensive Therapy ~60-70%	**Non-Intensive Therapy** ~30-40%	**Currently Untreated**
Intensive therapy + novel therapies (targeted & non-targeted)	Non-intensive therapy + novel therapies (targeted & non-targeted)	Single agent novel therapies (targeted & non-targeted)
Increase cure rate	Prolong EFS/OS	Clinical benefit

Sources: SEER. Cancer Stat Facts: AML 2015 and Epiphany EPIC oncology numbers; American Cancer Society. AML 2017.

Encouraging Phase 1 Data in Combination with Intensive Chemo Supports Label Enabling Phase 3 Study



PHASE 1 7+3 COMBO DATA

(TIBSOVO® cohort)

- Median age 63 years
- 70% de novo; 30% sAML
- Safety consistent with previously reported data
- 91% CR+CRi/CRp rate for de novo patients (31 of 34)
- 80% CR+CRi/CRp rate for all patients (39 of 49)

NEXT STEPS

HOVON 150 AML / AMLSG 29-18 PHASE 3 STUDY

Planned for Q1 2019 Initiation

BROAD IST SUPPORT

VYXEOS™ Combination

Sources: SEER. Cancer Stat Facts: AML 2015 and Epiphany EPIC oncology numbers; American Cancer Society AML 2017; ASCO 2018; ASH 2018; VYXEOS™ is a trademark of Jazz Pharmaceuticals

Compelling Phase 1 Combination Data for Patients Ineligible for Intensive Chemo Suggests Potential to Extend EFS/OS

~50K U.S. and EU Annual Newly Diagnosed AML Patients
IDH1/2m is ~20%

Treated Population

Intensive Therapy
~60-70%

Non-Intensive Therapy
~30-40%

Currently Untreated

PHASE 1 AZACITIDINE COMBO DATA

(TIBSOVO® cohort)
Updated Phase 1 Data Expected in 1H 2019

- Median age 76 years
- Safety consistent with previously reported data
- 78% ORR (18 of 23)
- 65% CR/CRi/CRp rate (15 of 23)
- 44% CR rate (10 of 23)
- 17/23 patients remain on therapy as of data cut off (median of 5 treatment cycles)

NEXT STEPS

AGILE PHASE 3 STUDY

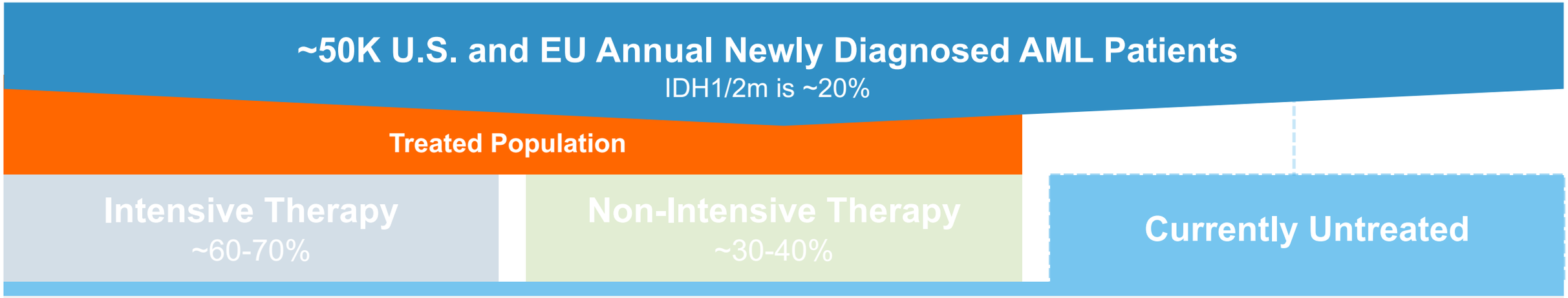
Enrollment Expected to Complete in 2020

BROAD IST SUPPORT

VENCLEXTA® Combination
XOSPATA® Combination
BEAT AML Master Trial

Sources: SEER. Cancer Stat Facts: AML 2015 and Epiphany EPIC oncology numbers; American Cancer Society AML 2017; ASCO 2018; VENCLEXTA® is a registered trademark of Abbvie; XOSPATA® is a registered trademark of Astellas

sNDA Submission Provides Potential to Offer Clinical Benefit to Patients with No Current Treatment Options



PHASE 1 SINGLE AGENT TIBSOVO® DATA

- Median age 76.5 years
- 79% sAML; 41% prior HMA
- Safety consistent with single agent data
- 58% ORR (19 of 33)
- 42% CR+CRh rate (14 of 33)
- 67% CR+CRh patients remain in response at 12 months

NEXT STEPS

sNDA APPROVAL

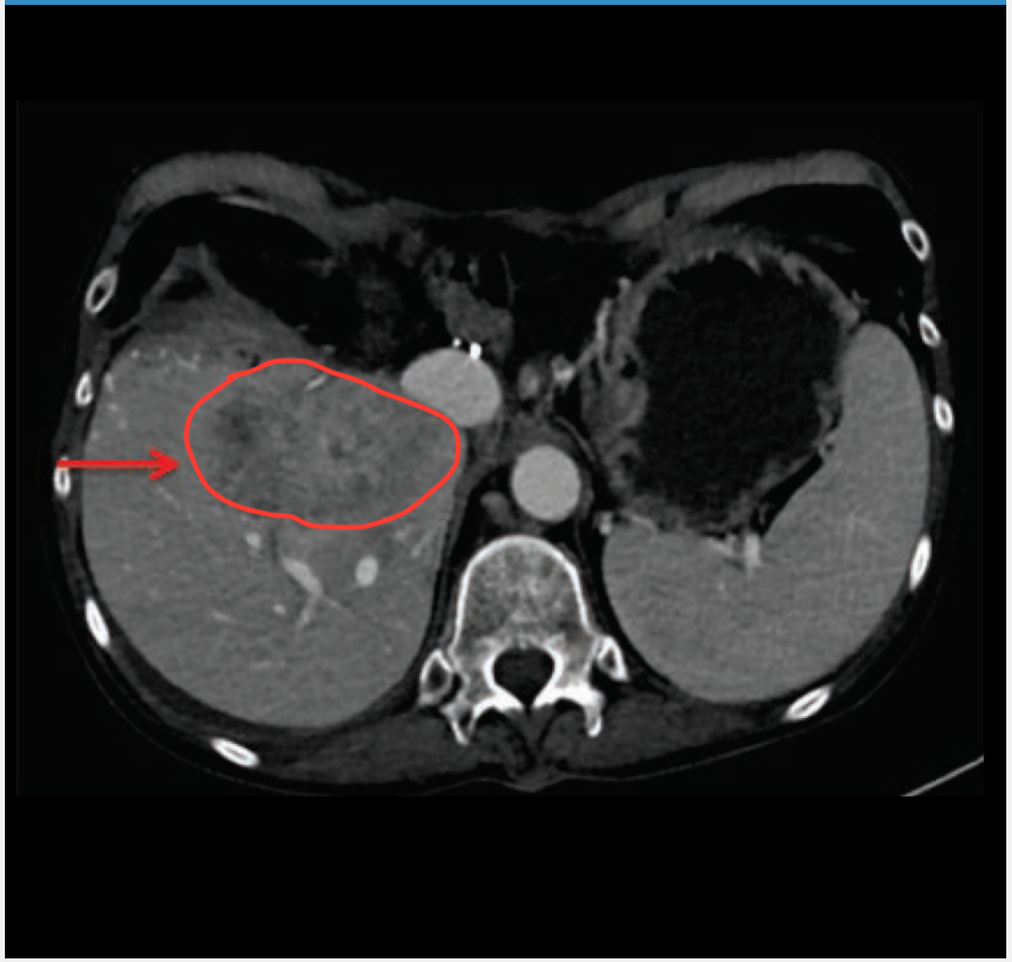
sNDA Submitted December 2018

Potential approval in 2019

Sources: SEER. Cancer Stat Facts: AML 2015 and Epiphany EPIC oncology numbers; American Cancer Society AML 2017; ASCO 2018; ASH 2018

Opportunity for an IDH1m Inhibitor in Solid Tumors

CHOLANGIOCARCINOMA



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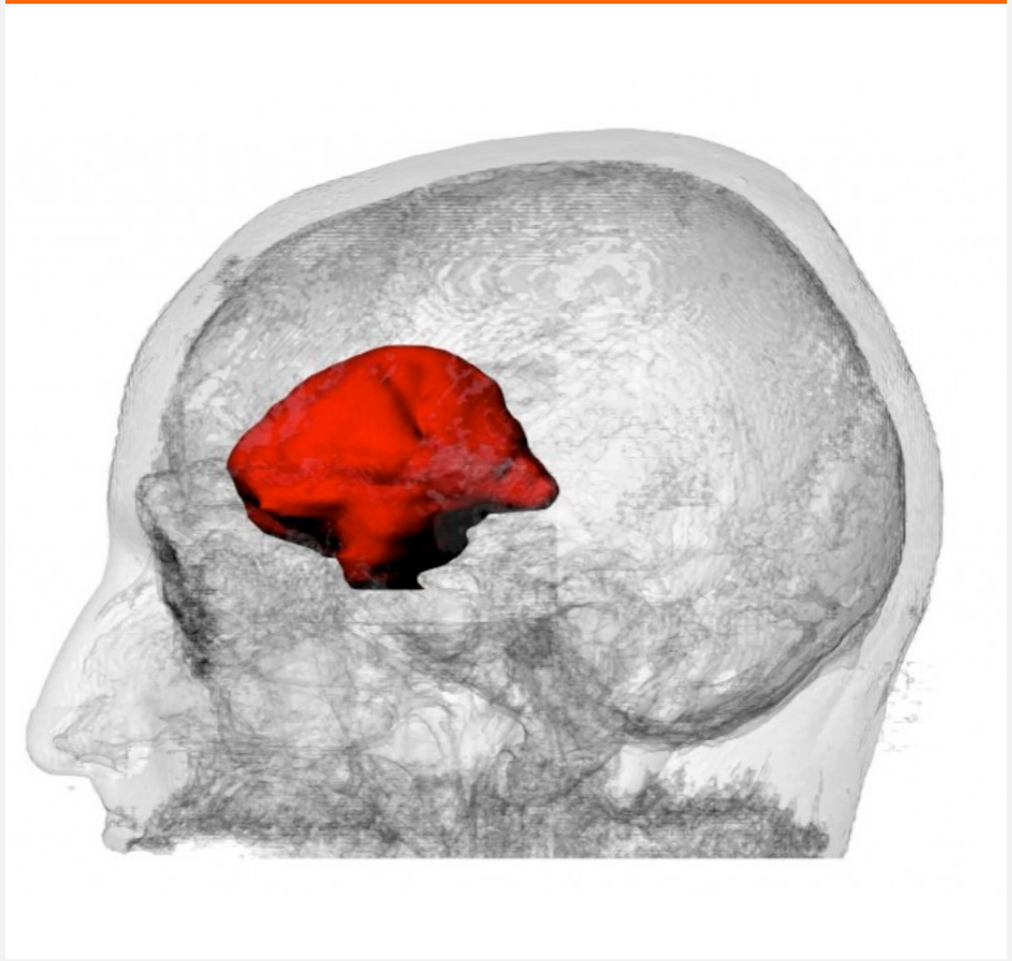
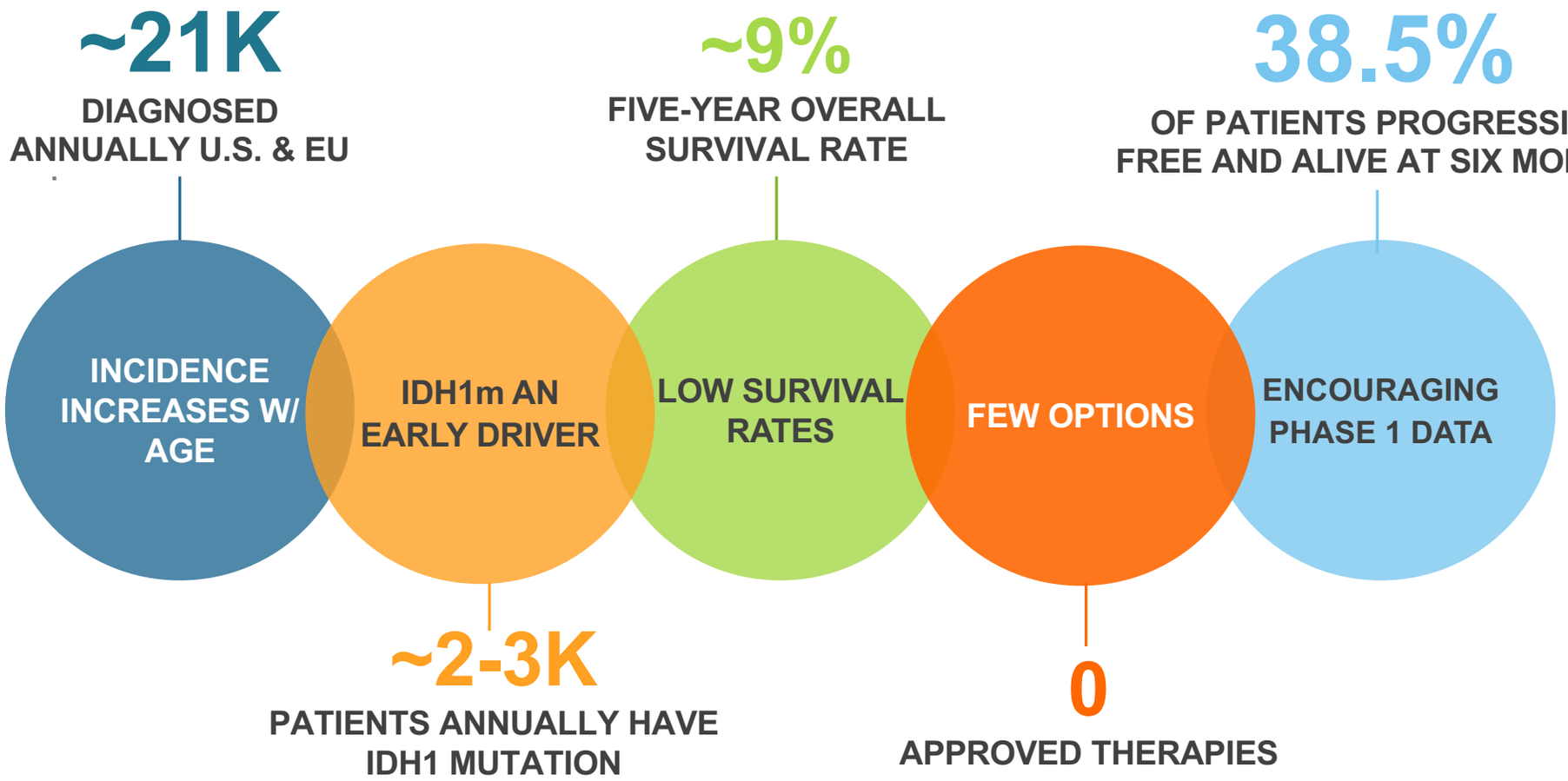
LOW GRADE GLIOMA



Sources: Steven Keating and Ahmed Hosny (right); Agios ASCO 2017 (left)

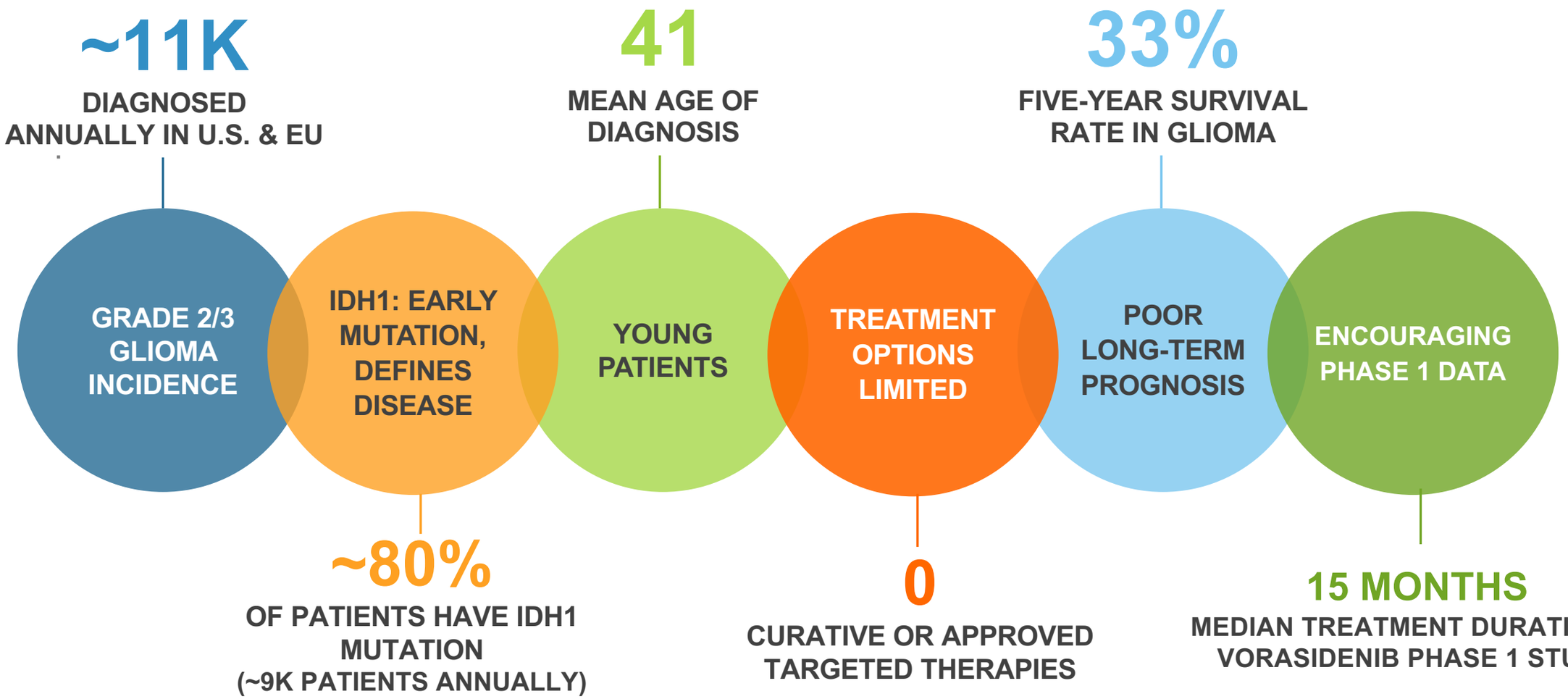
Plan to File sNDA for TIBSOVO® in Second-line or Later Cholangiocarcinoma by Year-end 2019



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; data from ASCO 2017

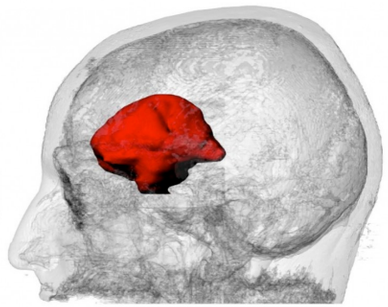
Topline data from the Phase 3 ClarIDHy study of TIBSOVO® in IDH1m advanced cholangiocarcinoma expected in 1H and full data to be presented in 2H 2019

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; SNO 2018

Current Treatment Paradigm for IDHm Gliomas



SURGERY

GLIOMA DIAGNOSIS

IDH1-mutant Glioma (~80%)

WHO GRADE II

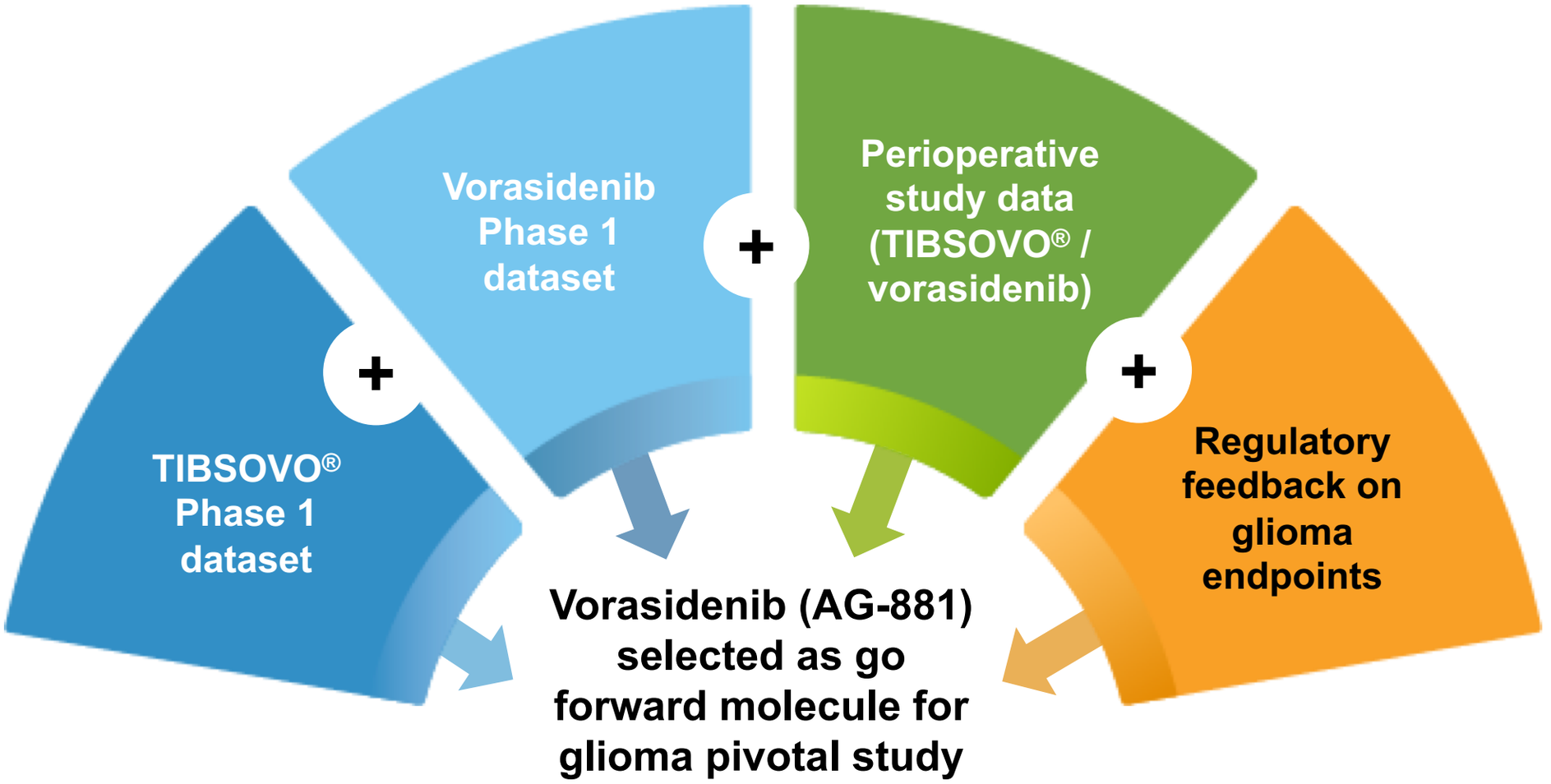
WATCH AND WAIT

WHO GRADE III

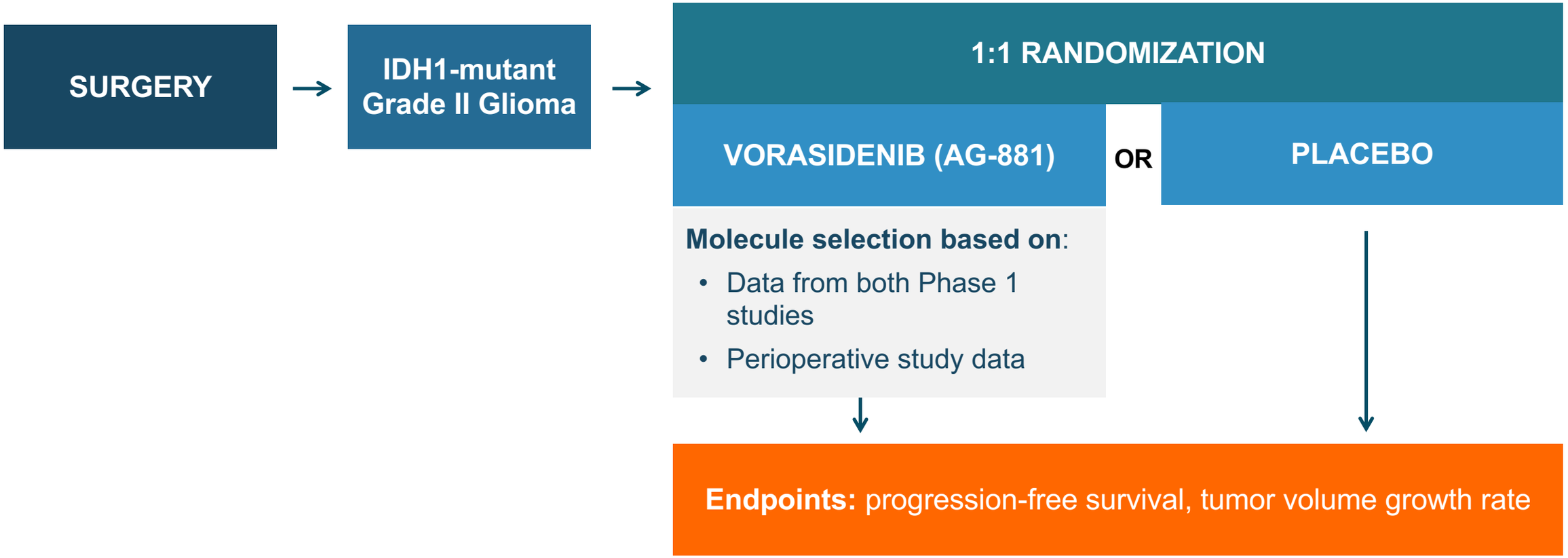
Radiotherapy → PCV (or temozolomide plus radiotherapy → temozolomide)

Sources: Steven Keating and Ahmed Hosny; N Engl J Med 2015; 372:2481-2498
PCV = procarbazine, lomustine and vincristine

Multiple Factors Guided Molecule Selection

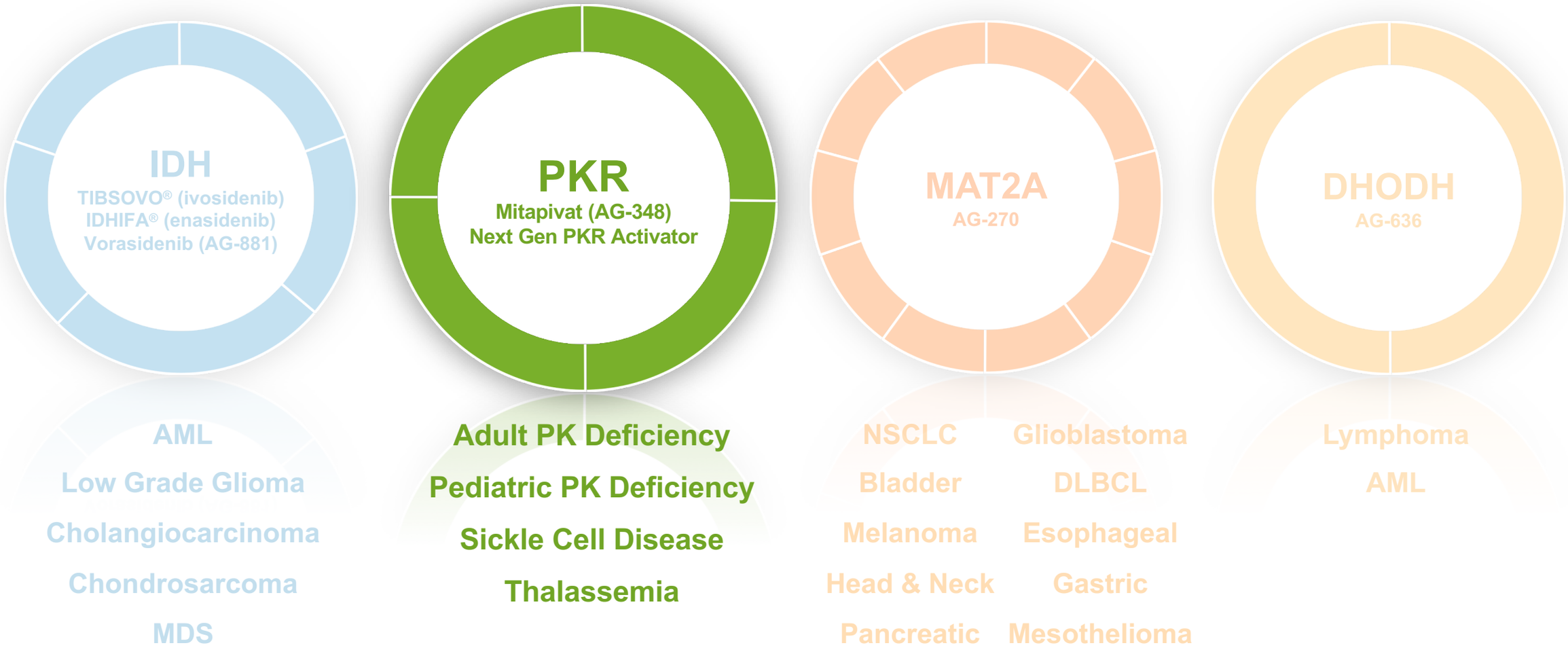


Pivotal Path in WHO Grade II Glioma: Aim to Delay Progression to Chemotherapy and/or Radiotherapy



Registration-enabling Phase 3 study of vorasidenib to initiate by year-end 2019; Perioperative data to be presented in 1H 2019

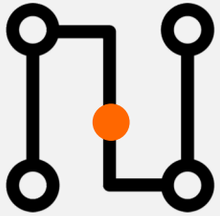
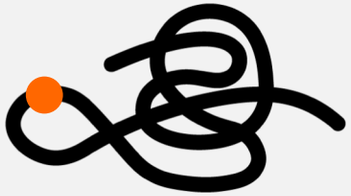
Productive Research & Discovery Engine Has Produced Four Key Targets with Multiple Disease Opportunities



Our Approach to Rare Genetic Diseases

Part of a New Wave of Transformational Therapies

Understanding and correcting the root cause of the disease

Tissue, organ, system	Disrupted metabolic networks	Mutated metabolic enzyme	DNA
			
Diverse pathophysiology and disease phenotypes	Toxic or deficient metabolites	Biochemical defects	Genetic mutation(s)
Palliative care	**Diet, scavenging, chelation, etc.**	**Enzyme replacement**	**Gene therapies**

Our Approach to Rare Genetic Diseases

Part of a New Wave of Transformational Therapies

Understanding and correcting the root cause of the disease

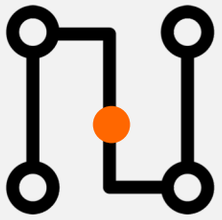
AGIOS APPROACH →

Disease-modifying small molecules targeting intracellular pathways leading to transformative outcomes for patients

Mutated metabolic enzyme

Biochemical defects

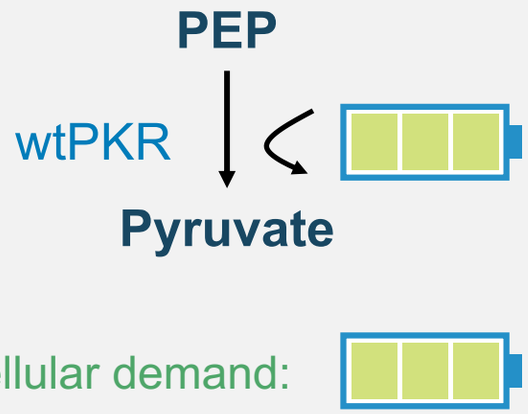
Disrupted metabolic networks



Toxic or deficient metabolites

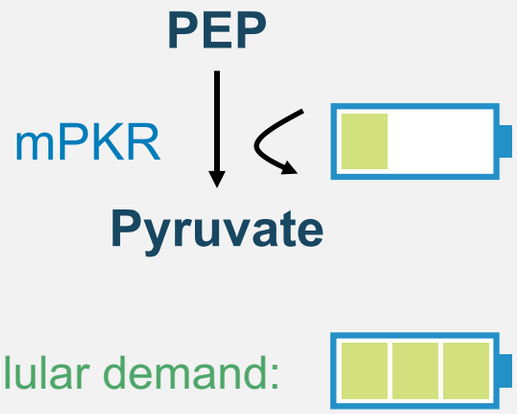
PK Activation Opportunities Across Hemolytic Anemias

Normal Red Cell



ATP production meets demand

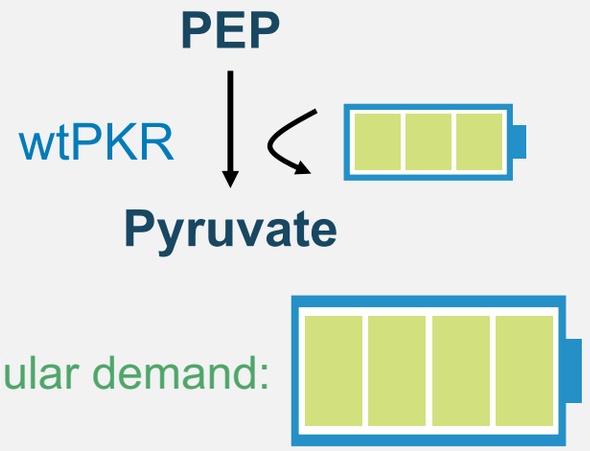
Pyruvate Kinase Deficiency



Inadequate production: ATP deficiency

✓ **Proof of concept achieved**

Other Hemolytic Anemias



Increased demand: ATP deficiency

Thalassemia Phase 2 initiated; planning underway in sickle cell disease

What's Possible with PKR Activators

NOW

- Adult PK Deficiency

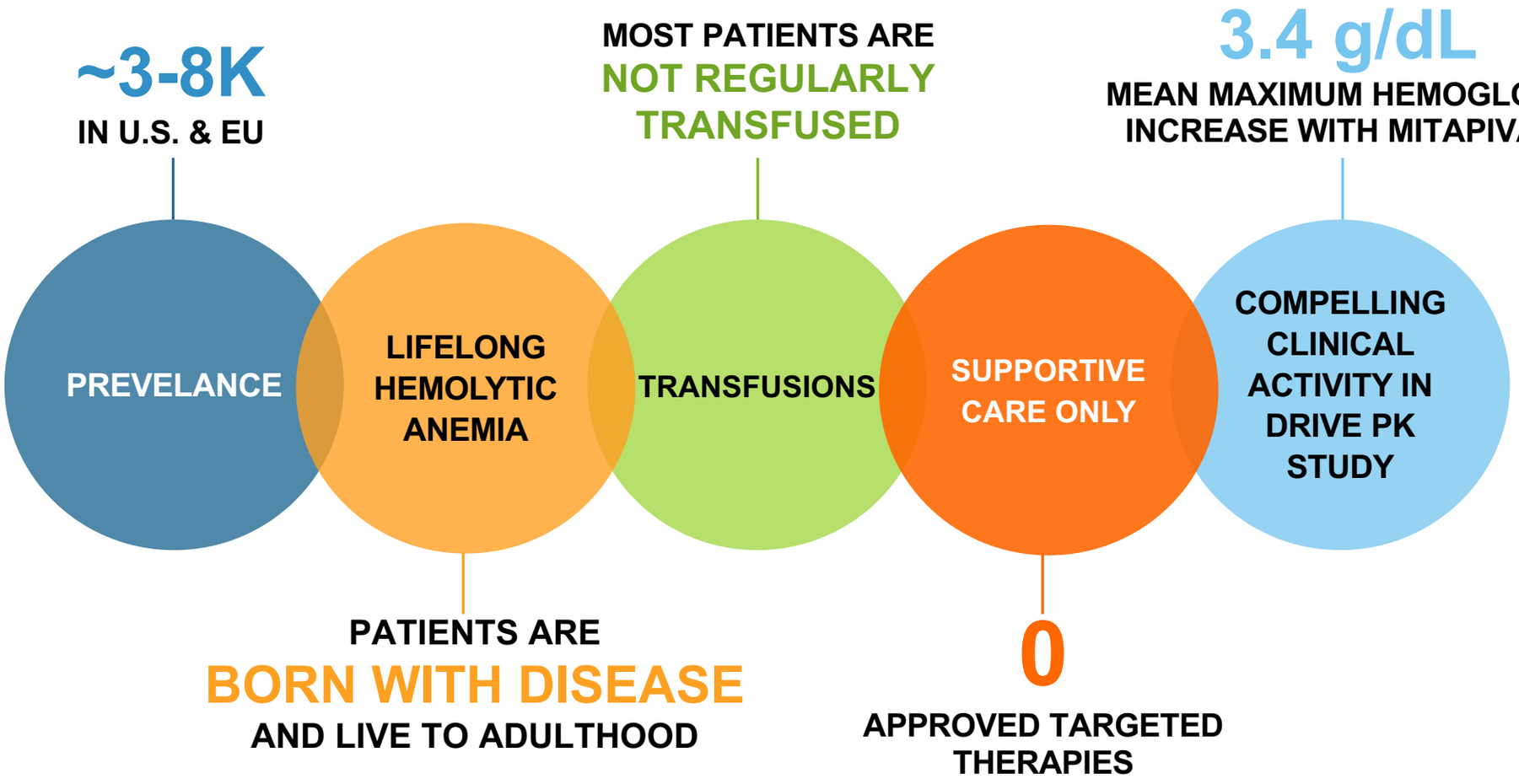
NEXT

- Thalassemia

FUTURE

- Pediatric PK Deficiency
- Sickle Cell Disease

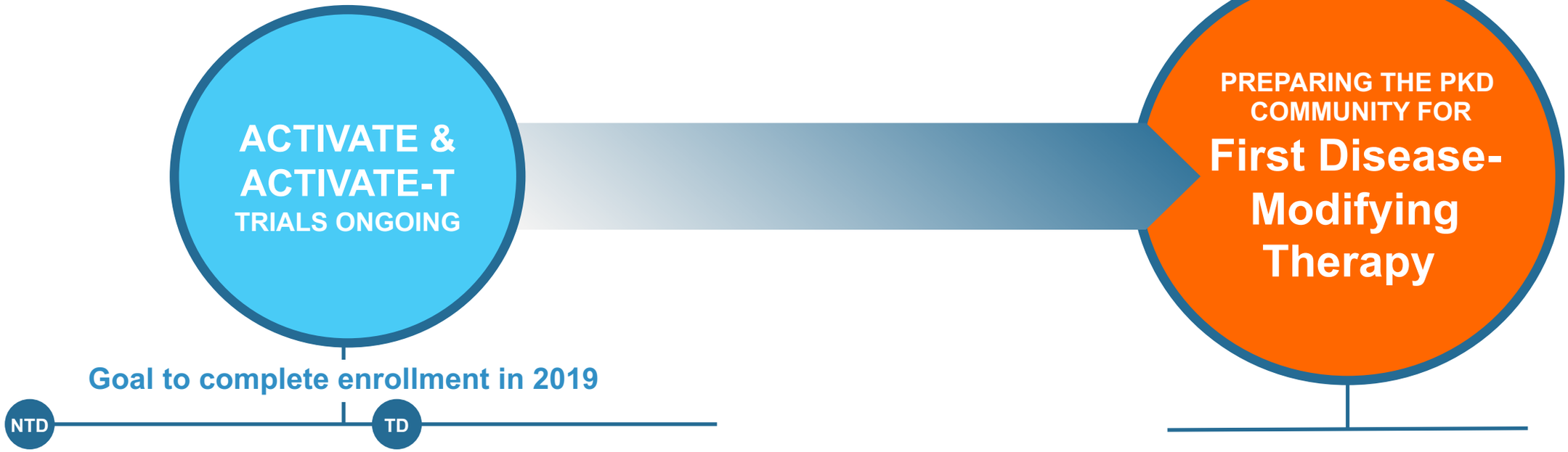
Opportunity for Mitapivat (AG-348) to be the First Disease-Modifying Treatment for PK Deficiency



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 who had a >1.0 g/dL increase in hemoglobin on study

Mitapivat Path to Approval: Potential First Disease-Modifying Therapy for Adult PK Deficiency



ACTIVATE

- **~80 patients** treated for 6 months
- **Primary endpoint:** portion of patients achieving 1.5 g/dL Hb increase over multiple visits

ACTIVATE-T

- **~20 patients,** minimum of 6 transfusions 1 year before enrollment
- **Primary endpoint:** reduction in transfusion burden over 6 months compared to patient's transfusion history

- **Disease awareness**
- **Improving path to diagnosis**
- **Patient voice**

Broadening the Opportunity for Mitapivat in Thalassemia and Pediatric Patients

PHASE 2 THALASSEMIA STUDY INITIATED

- ~20 non-transfusion dependent adults
- Evaluating 50 and 100 mg BID
- Primary endpoint: hemoglobin response (1.0 g/dL increase over baseline at 12 weeks)
- Goal to achieve proof of concept in 2019

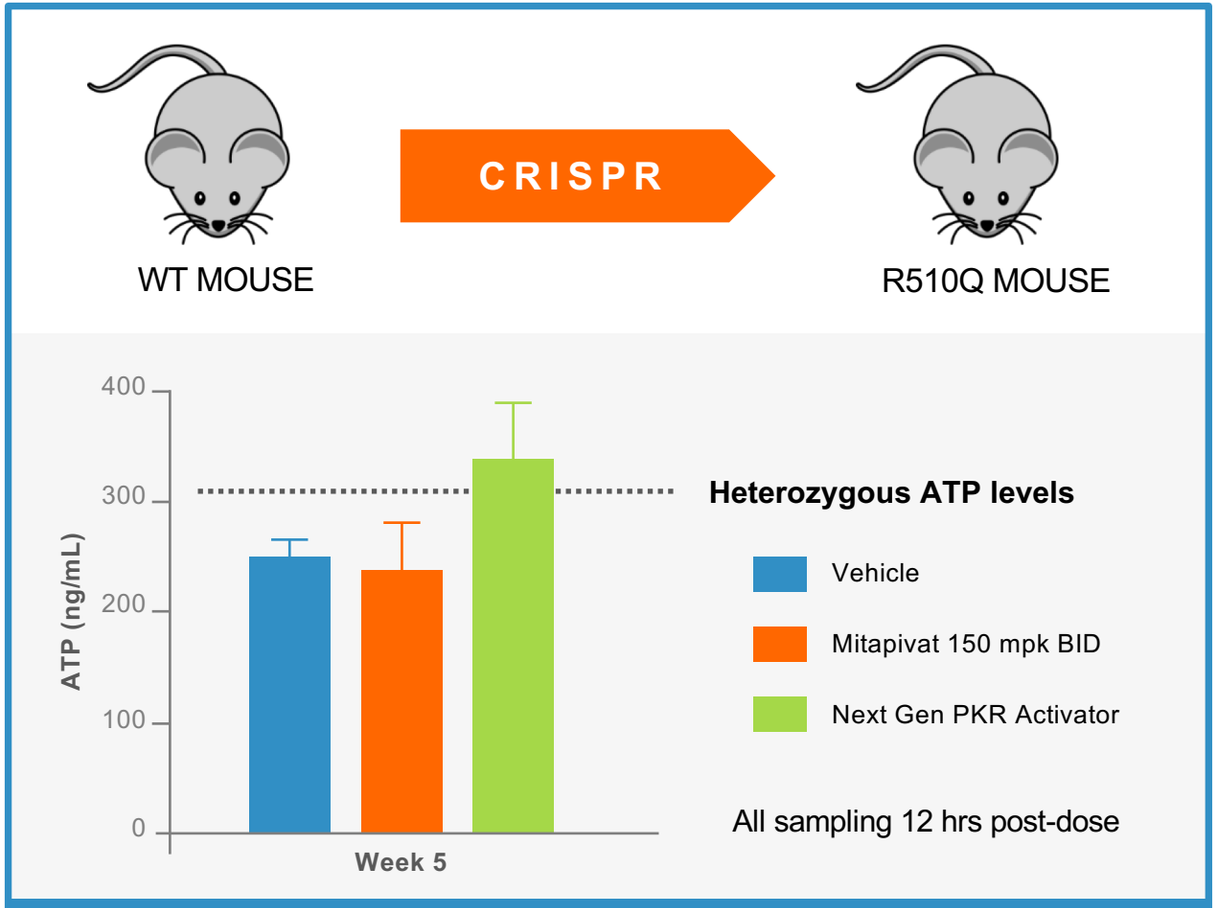
POTENTIAL PATH FORWARD FOR MITAPIVAT IN PEDIATRICS

- Safety and efficacy observed in DRIVE PK extension phase warrants evaluation of mitapivat in pediatric patients
- Juvenile toxicology studies underway
- Discussion with regulators planned for 2019
- Primary goal to develop mitapivat in a pediatric population

Committed to Continued Development of PKR Activators for the Treatment of Every Patient with PK Deficiency

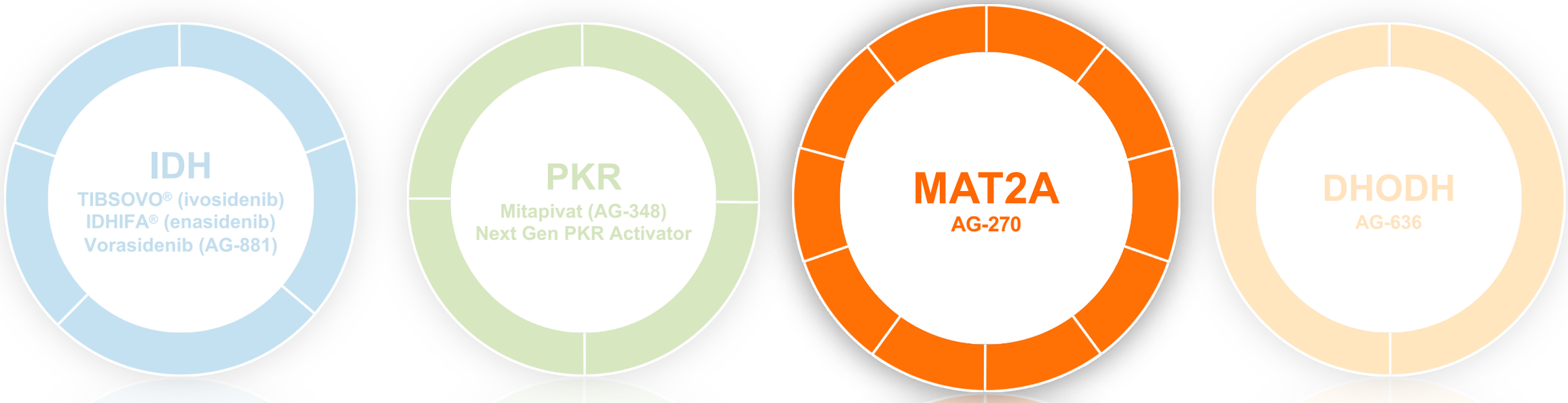
DEVELOPMENT CANDIDATE FOR A NEXT GENERATION PKR ACTIVATOR SELECTED

- More potent across a range of PKR mutations
- Address patients who do not have a sufficient response to mitapivat
- IND planned in next 12-18 months



Next generation molecule superior at increasing ATP levels in a mouse model with the R510Q mutation

Productive Research & Discovery Engine Has Produced Four Key Targets with Multiple Disease Opportunities



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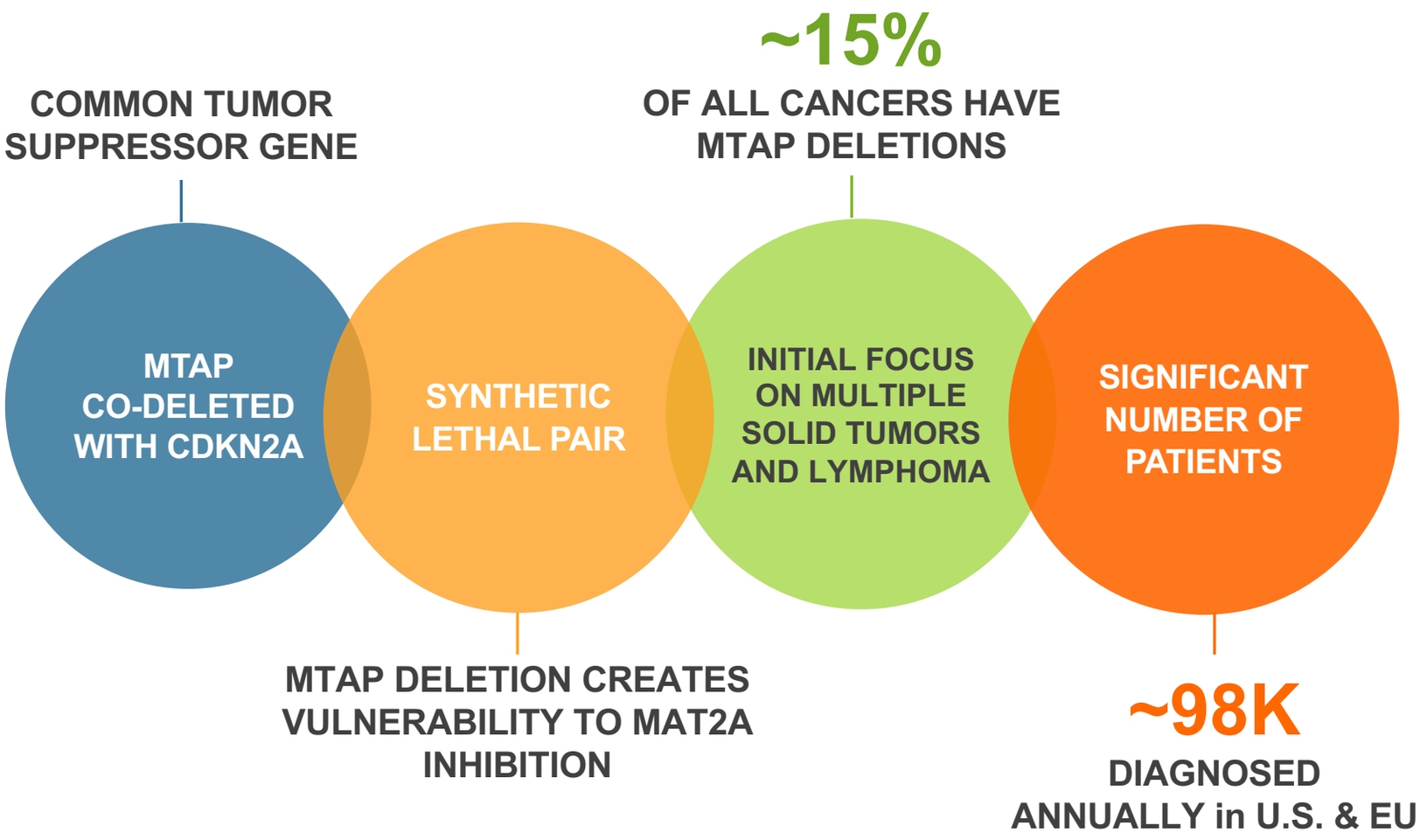
Adult PK Deficiency
Pediatric PK Deficiency
Sickle Cell Disease
Thalassemia

NSCLC
Glioblastoma
Bladder
DLBCL
Melanoma
Esophageal
Head & Neck
Gastric
Pancreatic
Mesothelioma

Lymphoma
AML

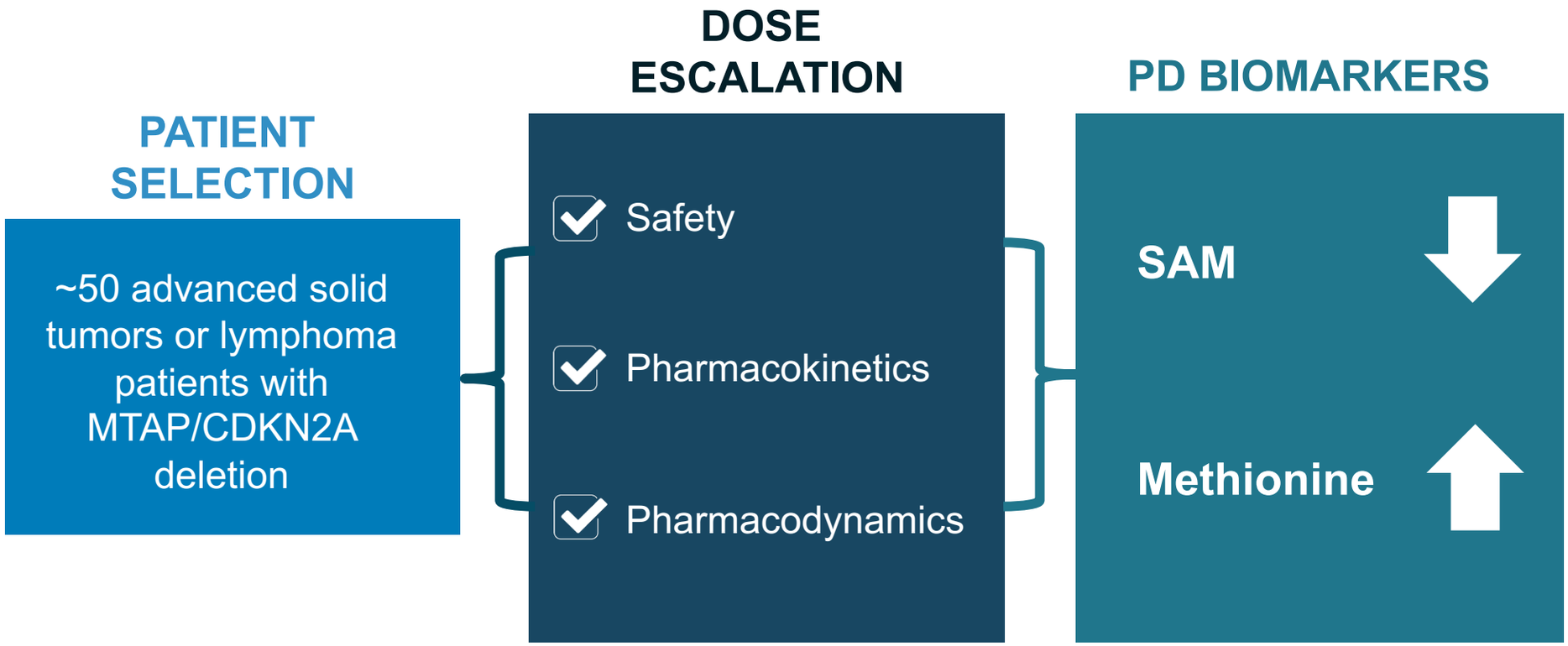
MAT2A Inhibitor AG-270 Leverages Vulnerability Created by the Most Frequently Deleted Metabolic Gene in Cancer



Sources: US Incidence data is from the NCI SEER; MTAP deletion frequencies are from Agios analysis of data from The Cancer Genome Atlas; Marjon et al Cell Reports. 2016 Apr 19;15(3):574-587

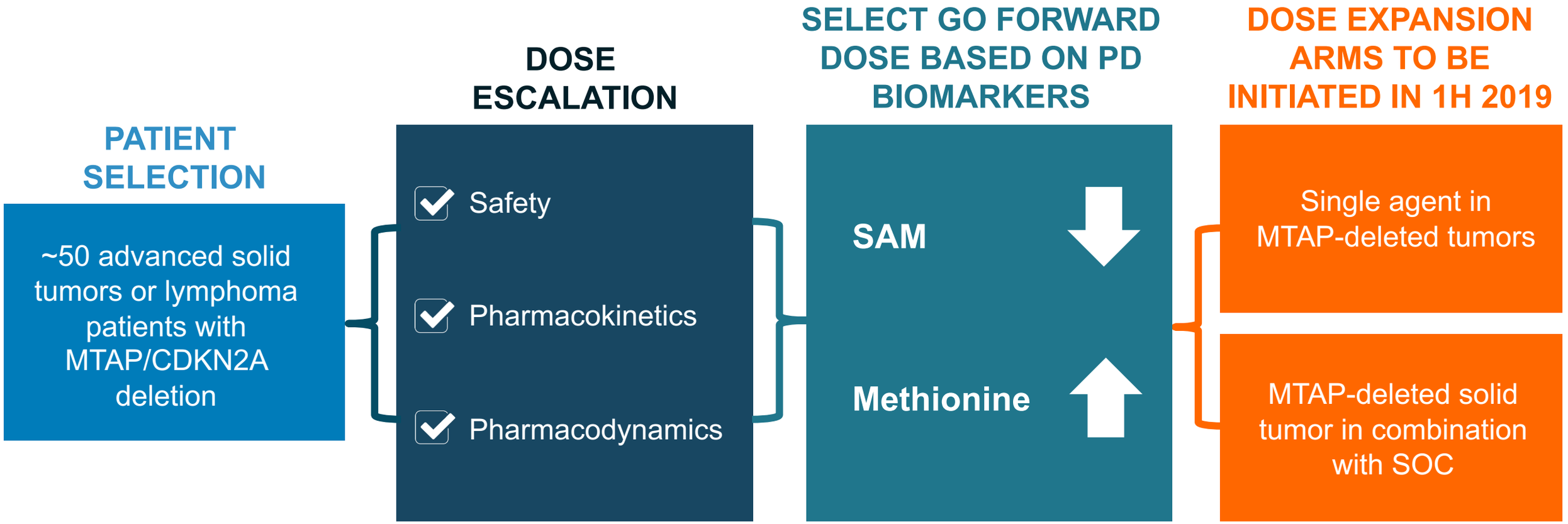
Initiating dose-expansion arms in 1H;
First clinical data from Phase 1 dose-escalation trial expected in 2H 2019

First Clinical Data Presentation to Focus on PD Biomarkers



First clinical data from the AG-270 Phase 1 dose-escalation expected in 2H 2019

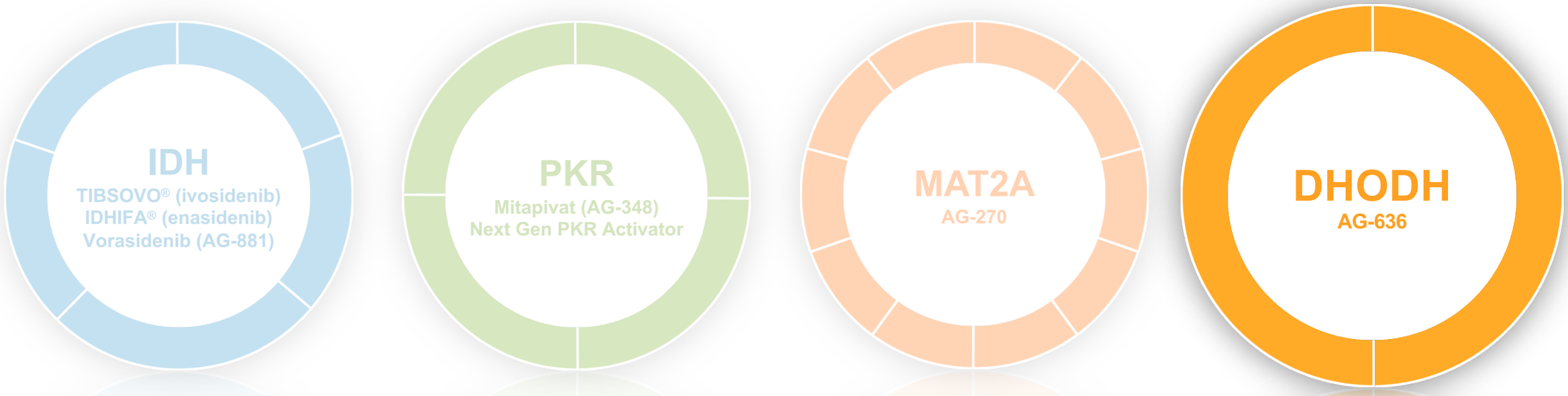
Advancing AG-270 to Next Phase of Clinical Development



ClinicalTrials.gov Identifier: NCT03435250

Updated preclinical data for AG-270 to be presented in 1H 2019

Productive Research & Discovery Engine Has Produced Four Key Targets with Multiple Disease Opportunities

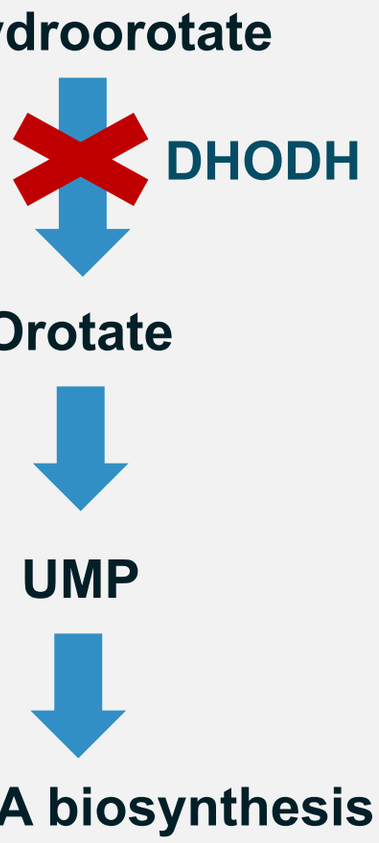


AML	Adult PK Deficiency	NSCLC	Glioblastoma
Low Grade Glioma	Pediatric PK Deficiency	Bladder	DLBCL
Cholangiocarcinoma	Sickle Cell Disease	Melanoma	Esophageal
Chondrosarcoma	Thalassemia	Head & Neck	Gastric
MDS		Pancreatic	Mesothelioma

Lymphoma
AML

Phase 1 Study of DHODH Inhibitor AG-636 in Lymphoma

DHODH catalyzes a critical step in pyrimidine biosynthesis



LYMPHOMA

Phase 1 Study in Treatment Refractory Lymphoma

Planned for 1H 2019

Dose Escalation

- Determine MTD
- PK and PD to guide dose and schedule
- Safety and tolerability
- Evaluation of anti-lymphoma activity

Dose Expansion

- Confirm safety of Phase 2 dose
- Further assessment of anti-lymphoma activity

ACUTE MYELOID LEUKEMIA

Phase 1 Study in Treatment Refractory AML Planned

Agios Preclinical Pipeline

Program	Target Discovery	Target Validation	Drug Discovery	Drug Candidate
Oncology				
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

What's New Today: 2019 Key Milestones & Data Presentations Position Agios for Long-term Value Creation

Key 2019 Milestones

- Potential FDA approval and commercialization of monotherapy TIBSOVO® in untreated AML in 2019
- Complete AG-270 Phase 1 dose-escalation and initiate expansion arms in 1H 2019
- Initiate AG-636 Phase 1 dose-escalation trial in lymphoma in 1H 2019
- Achieve proof-of-concept for mitapivat in thalassemia in 2H 2019
- Submit sNDA for TIBSOVO® in second line or later cholangiocarcinoma by year-end
- Initiate glioma registration-enabling trial with vorasidenib by year-end
- Complete enrollment in PK deficiency pivotal trials ACTIVATE-T and ACTIVATE by year-end

Key Data Presentations

- Updated data from Phase 1 combo trial of TIBSOVO® with azacitidine in newly diagnosed AML in 1H 2019
- Data from perioperative 'window' trial with TIBSOVO® and vorasidenib in IDHm low-grade glioma in 1H 2019
- Topline data from Phase 3 ClarIDHy trial of TIBSOVO® in IDH1m advanced cholangiocarcinoma to be reported in 1H and full data to be presented in 2H 2019
- Data from dose-escalation portion of Phase 1 trial of AG-270 in MTAP-deleted tumors in 2H 2019

Thank You