



AgiOS Investor Presentation

November 2019

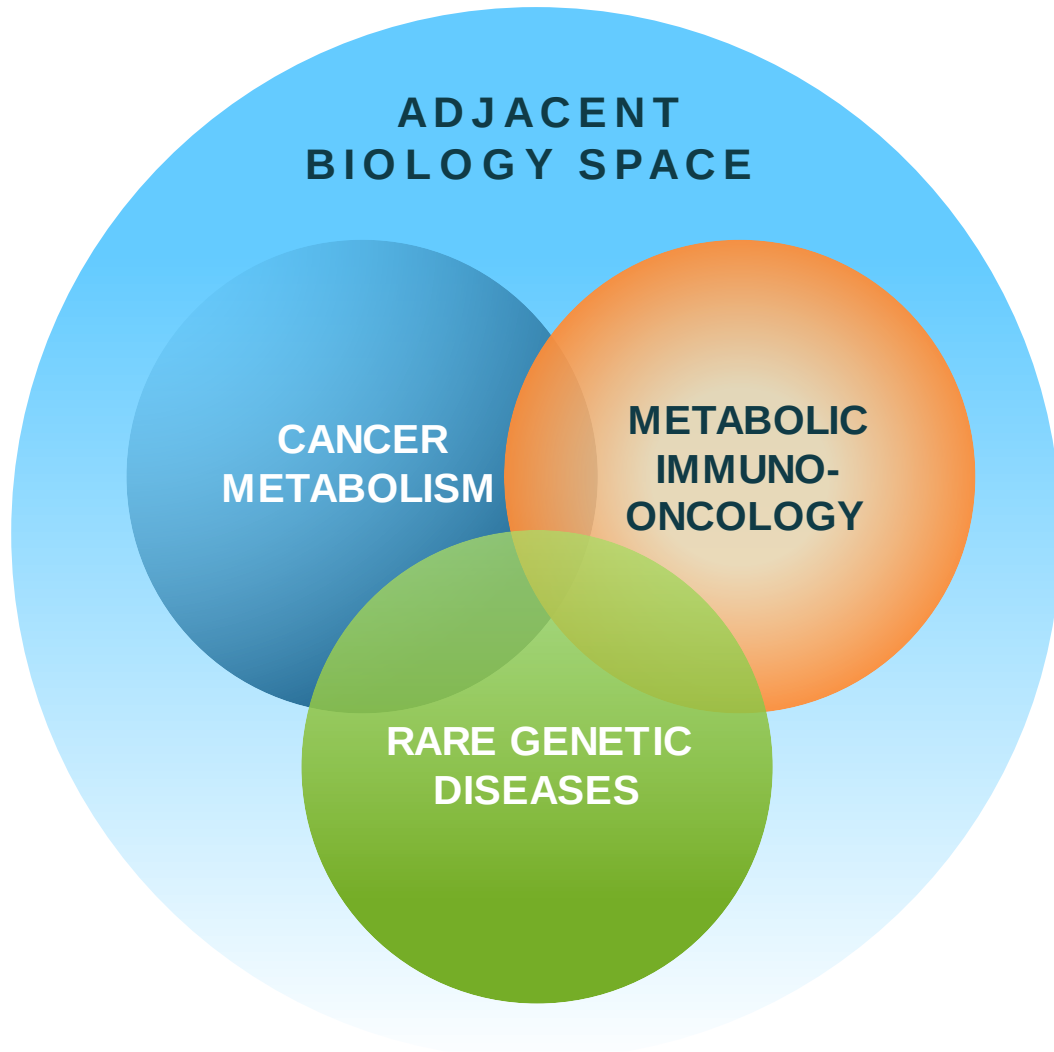


Forward Looking Statements

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 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," "building," "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.



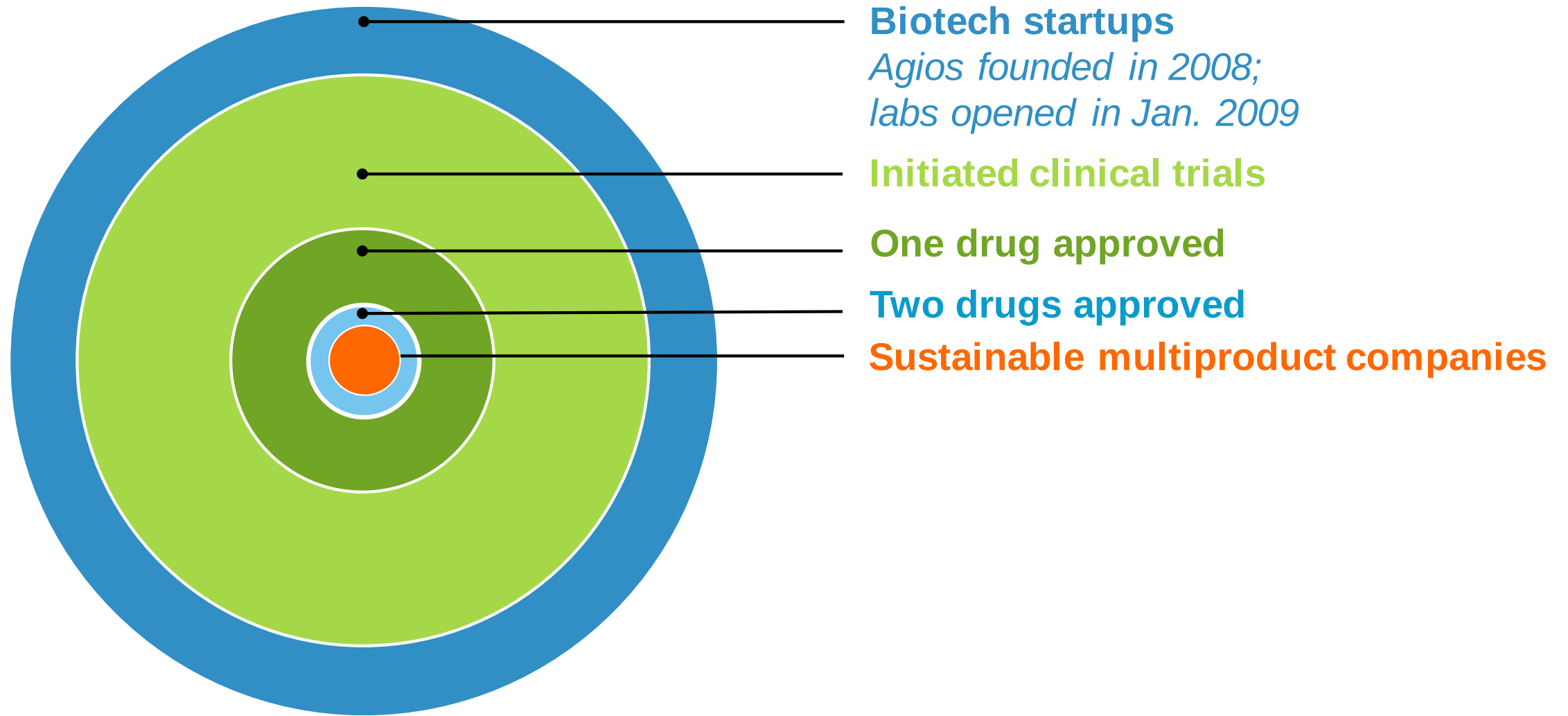
Driven By a Clear Vision and Values



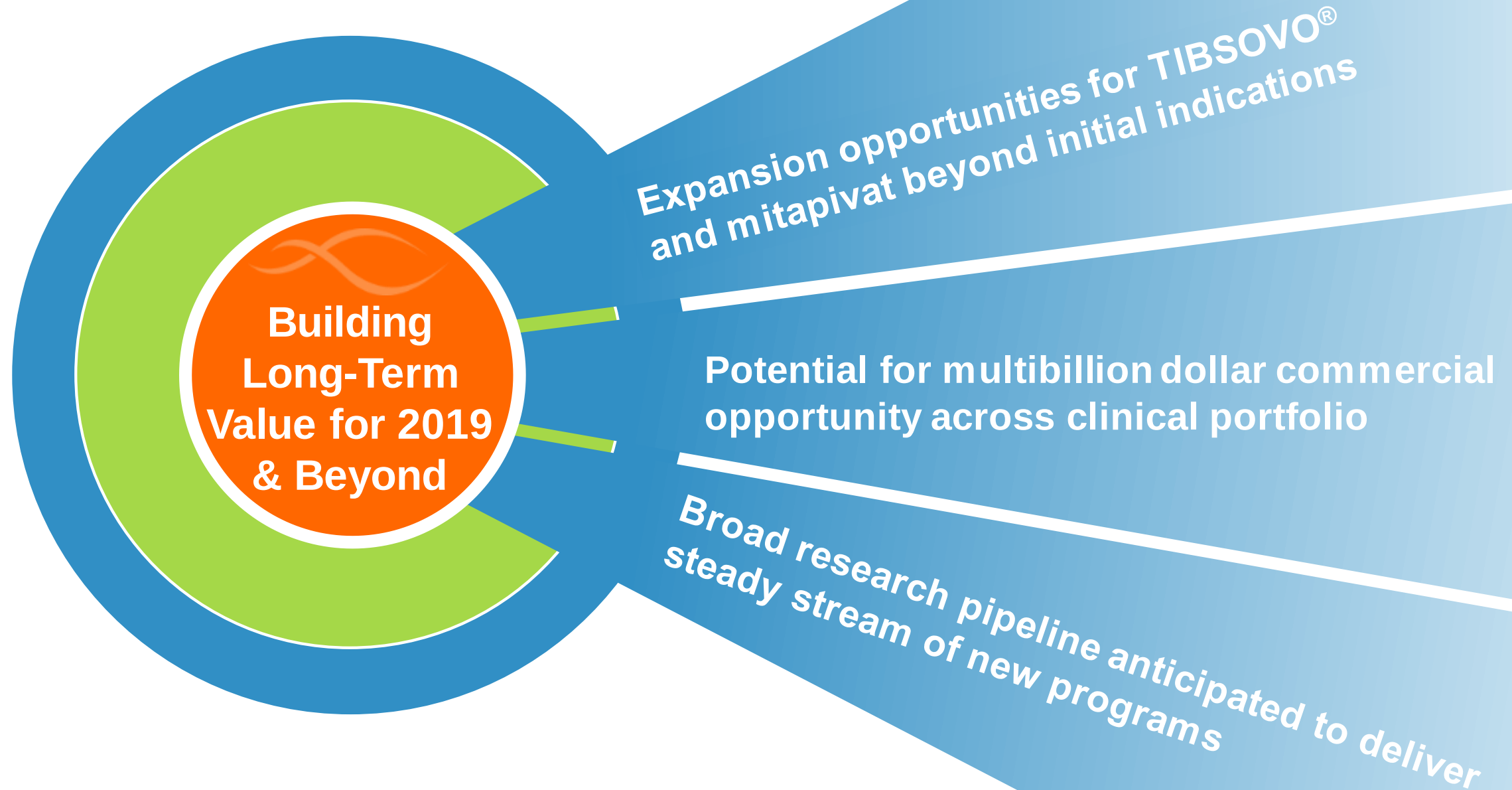
AgiOS is passionately committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and rare genetic diseases.



Building One of the Next Great Pharmaceutical Companies



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



500+

EMPLOYEES

1

VISION

8

DISEASES



6

PIVOTAL CLINICAL TRIALS

9

ADDITIONAL CLINICAL TRIALS



2

MEDICINES
APPROVED

+

4

ADDITIONAL COMPOUNDS
IN CLINICAL DEVELOPMENT

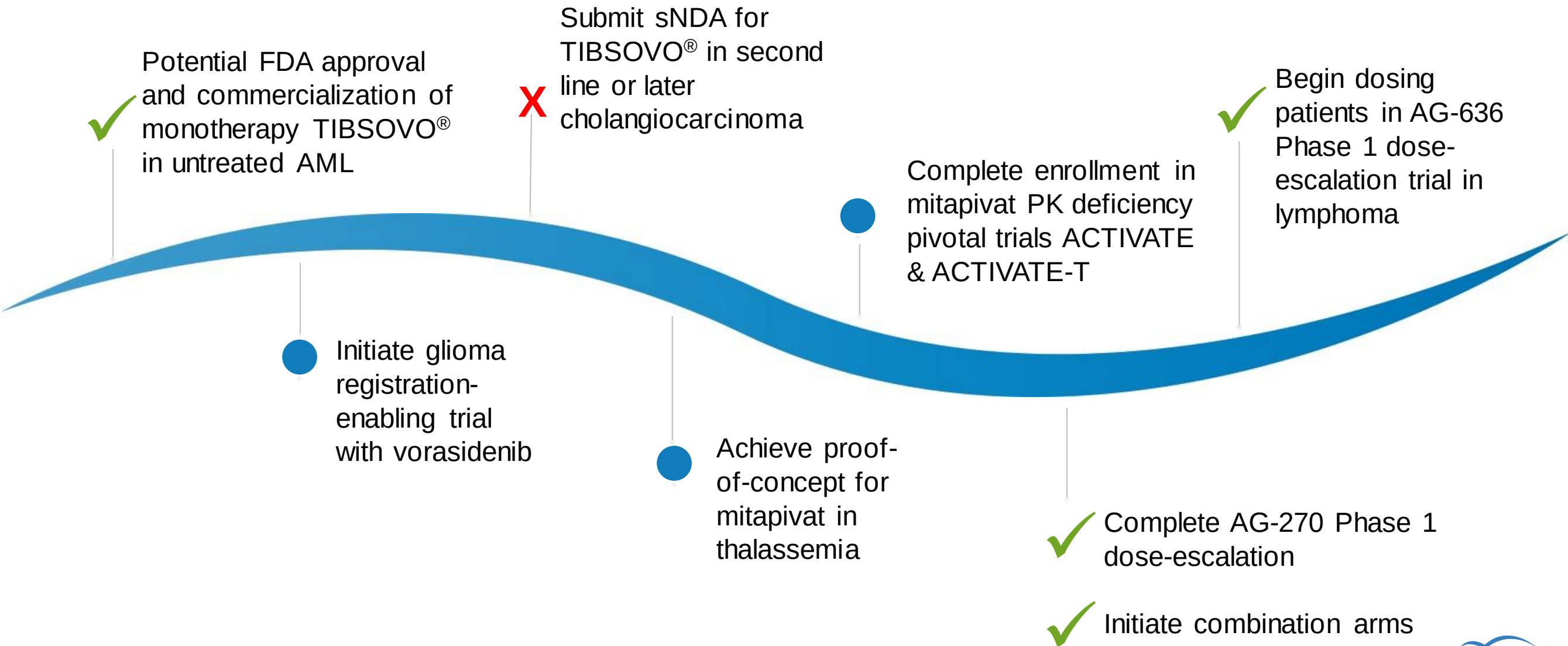


Agios Clinical Pipeline

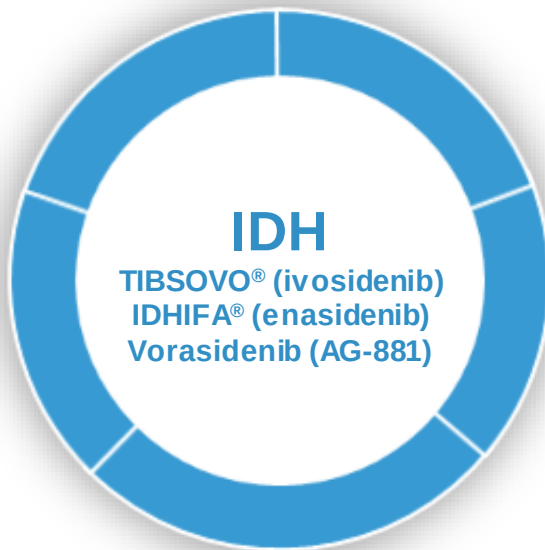
IC = Intensive Chemotherapy

CLINICAL PROGRAMS	INDICATION	DRUG DISCOVERY	EARLY STAGE CLINICAL DEVELOPMENT	LATE STAGE CLINICAL DEVELOPMENT	REGULATORY SUBMISSION	APPROVED	PRIMARY RIGHTS
TIBSOVO® ivosidenib (IDH1m inhibitor)	R/R AML		Phase 1 Dose-Escalation and Expansion		EU	U.S.	
	Frontline AML Monotherapy		Phase 1 Dose-Escalation and Expansion			U.S.	
	IC Eligible Frontline AML		Phase 1b 7+3 Combo	Phase 3 HOVON 7+3 Combo			
	IC Ineligible Frontline AML		Phase 1/2 Azacitidine Combo	Phase 3 AGILE Azacitidine Combo			
	Cholangio		Phase 1 Dose-Escalation and Expansion	Phase 3 ClarIDHy			
	Glioma		Perioperative Study				
IDHIFA® enasidenib (IDH2m inhibitor)	R/R AML			Phase 3 IDHENTIFY	EU	U.S.	  Agios U.S. Co-promotion and Royalty
	IC Eligible Frontline AML		Phase 1b 7+3 Combo	Phase 3 HOVON 7+3 Combo			
	IC Ineligible Frontline AML		Phase 1/2 Azacitidine Combo				
Mitapivat (PKR activator)	Transfusion Independent PK Deficiency		Phase 2 DRIVE PK	Phase 3 ACTIVATE			
	Transfusion Dependent PK Deficiency			Phase 3 ACTIVATE-T			
	Thalassemia		Phase 2 Study				
Vorasidenib (brain-penetrant, pan-IDHm inhibitor)	Glioma		Perioperative Study	Phase 3 Study Planned for 4Q 2019			
	Solid Tumors		Phase 1 Dose-Escalation and Expansion				
AG-270 (MAT2A inhibitor)	MTAP-deleted Tumors		Phase 1 Dose-Escalation and Expansion				  Subject to Celgene Option Joint Worldwide Collaboration
AG-636 (DHODH inhibitor)	Lymphoma		Phase 1 Dose-Escalation				

2019 Key Milestones Position Agios for Long-term Value Creation



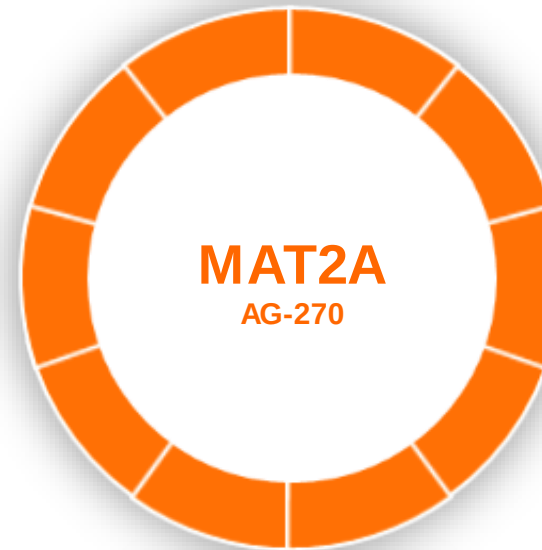
Productive Research & Discovery Engine Has Produced Four Key Targets with Multiple Disease Opportunities



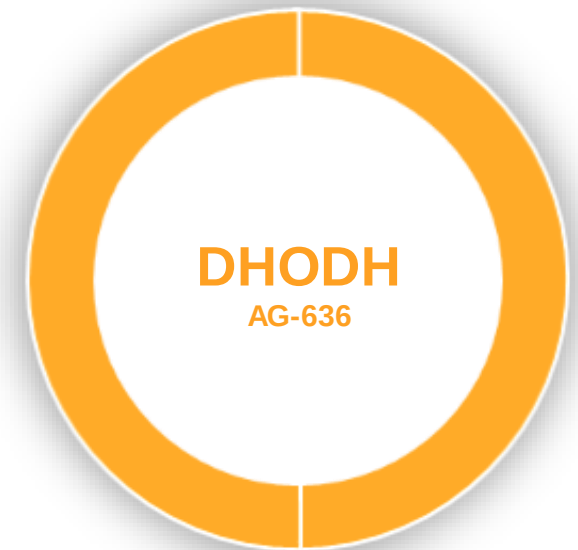
AML
Low Grade Glioma
Cholangiocarcinoma
Chondrosarcoma
MDS



Adult PK Deficiency
Pediatric PK Deficiency
Sickle Cell Disease
Thalassemia



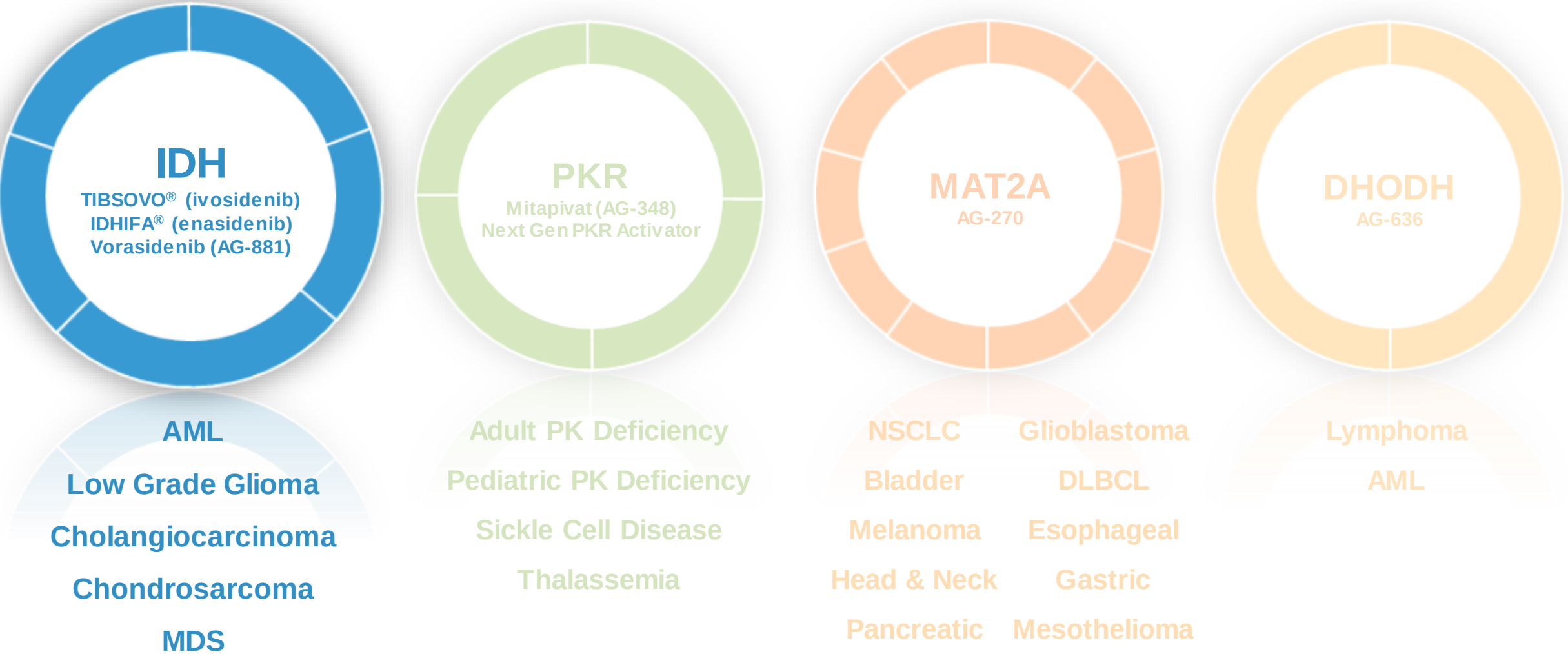
NSCLC Glioblastoma
Bladder DLBCL
Melanoma Esophageal
Head & Neck Gastric
Pancreatic Mesothelioma



Lymphoma
AML



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



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



\$27M

Q3 2019 Worldwide Net Sales
U.S. Co-commercialization with Celgene



\$17.4M

Q3 2019 U.S. Net Sales



MAA

Submitted & Validated



~90%

Physicians Testing for
IDH1/IDH2 mutations



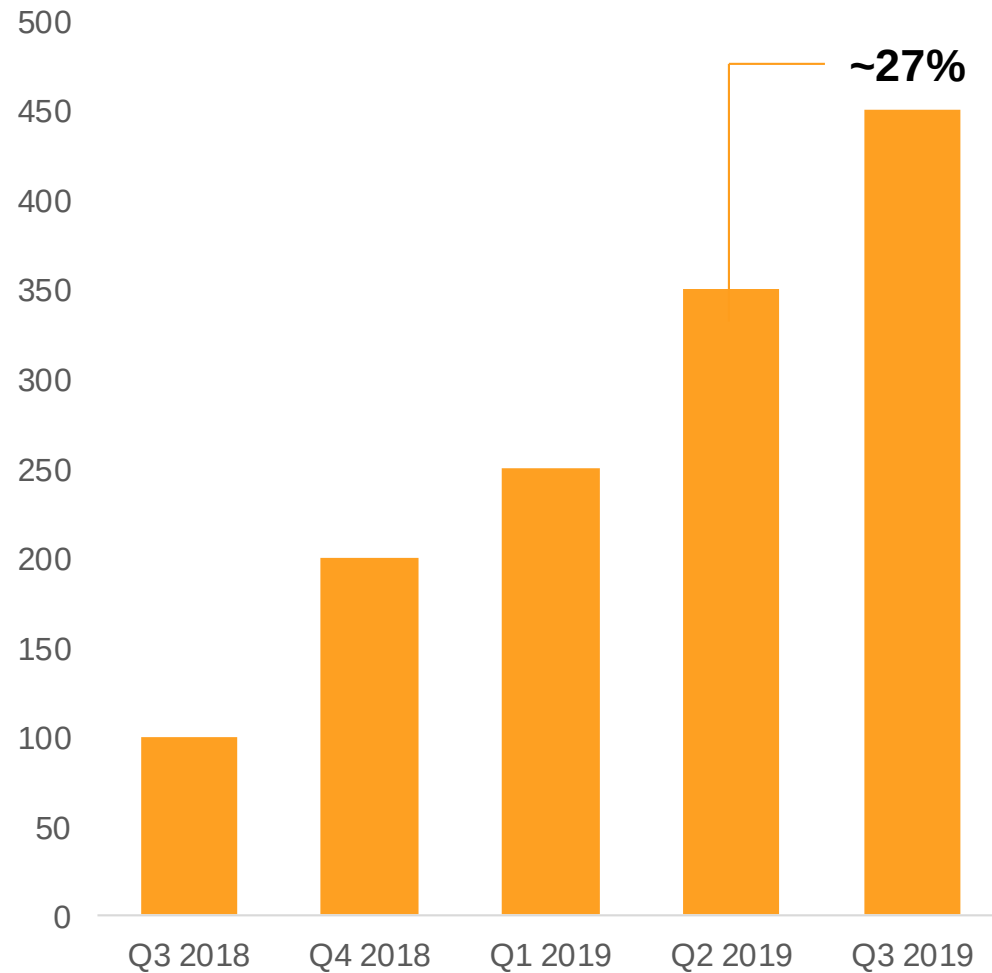
~450

Unique Prescribers
as of Q3

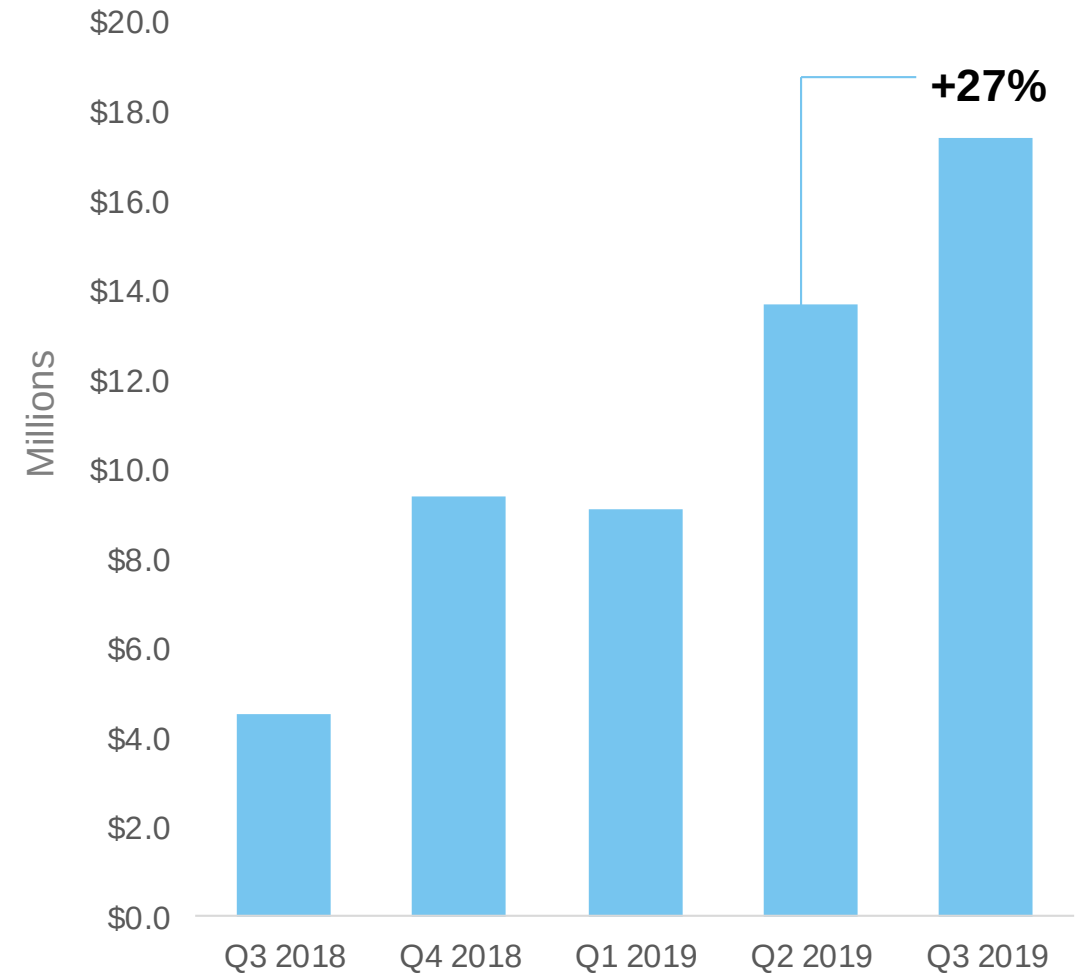


Demonstrated Ability to Drive Commercial Performance in R/R and Newly Diagnosed AML

Unique Prescribers



TIBSOVO® Revenue



Shifting the Current Treatment Paradigm for Patients with Newly Diagnosed IDH1m AML

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

Intensive Therapy

~60-70% Treated Patients

Intensive therapy
+ novel therapies
(targeted & non-targeted)

Increase cure rate

Non-Intensive Therapy

~30-40% Treated Patients

Eligible for
Combination Therapy

Combination of non-intensive
therapy + novel therapies
(targeted & non-targeted)

Prolong EFS/OS

Not Eligible for
Combination Therapy

Single agent novel therapies
(targeted & non-targeted)

Prolong EFS/OS

Untreated

Up to ~25% all
Patients

Single agent
novel therapies
(targeted & non-
targeted)

Clinical benefit



Potential to Offer Clinical Benefit to Newly Diagnosed Patients Ineligible for Intensive Chemotherapy

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

Intensive Therapy

Non-Intensive
Combination Therapy

Non-Intensive
Monotherapy

SINGLE AGENT TIBSOVO® FDA APPROVED IN NEWLY DIAGNOSED AML

TIBSOVO® indicated for use in adult patients with newly diagnosed AML with an IDH1 mutation who are ≥ 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.

Results from 28 Patients in the Phase 1 Study:

- Median age 77 years
- 79% had AML-MRC or therapy-related AML; 46% prior HMA
- Safety consistent previously reported data
- 29% CR rate
- 43% CR+CRh rate
- 58.3% of CR+CRh patients were in remission at 1 year after receiving treatment



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%

Intensive Therapy

**Non-Intensive
Combination Therapy**

Non-Intensive
Monotherapy

PHASE 1 AZACITIDINE COMBO DATA

(TIBSOVO® cohort)

Received Breakthrough Therapy Designation

- Median age 76 years
- Safety consistent with previously reported data
- 78% ORR (18 of 23)
- 82% 12-month overall survival rate
- 70% CR+CRh rate (16 of 23)
- 61% CR rate (14 of 23)
- Median duration of CR (95% CI 9.3, NE) and CR+CRh (95% CI 12.2, NE) not reached

NEXT STEPS

AGILE PHASE 3 STUDY

Enrollment Expected to Complete in 2020

BROAD IST SUPPORT

VENCLEXTA® Combination
XOSPATA® Combination
BEAT AML Master Trial



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

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

Intensive Therapy

**Non-Intensive
Combination Therapy**

**Non-Intensive
Monotherapy**

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**
Trial initiated

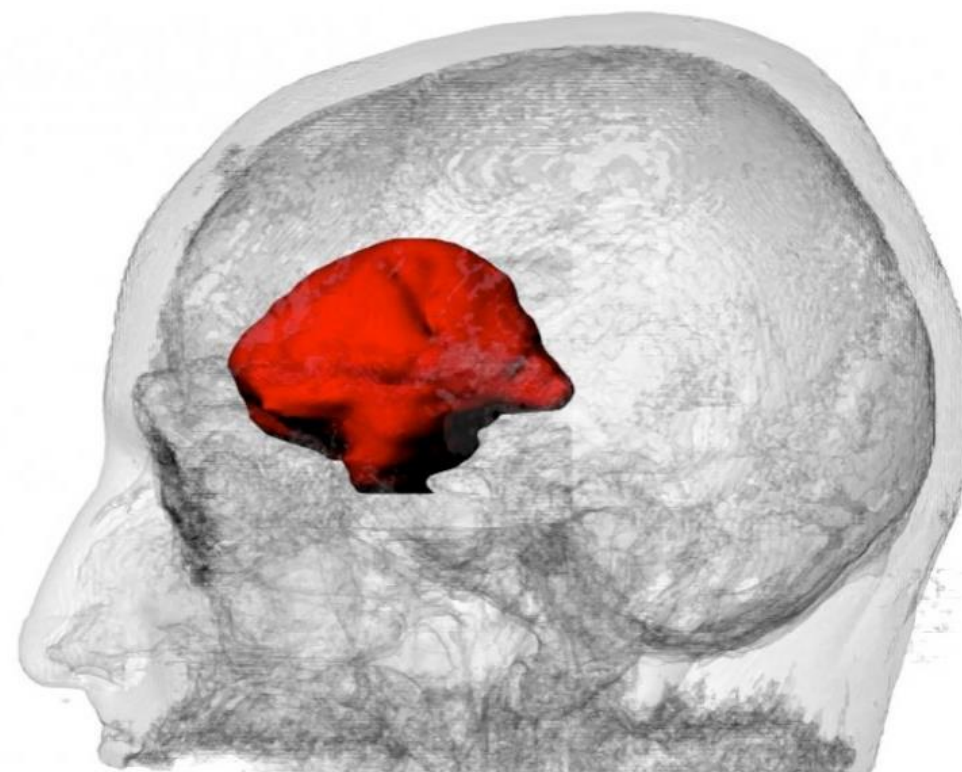
BROAD IST SUPPORT
VYXEOS™ Combination

Opportunity for an IDH1m Inhibitor in Solid Tumors

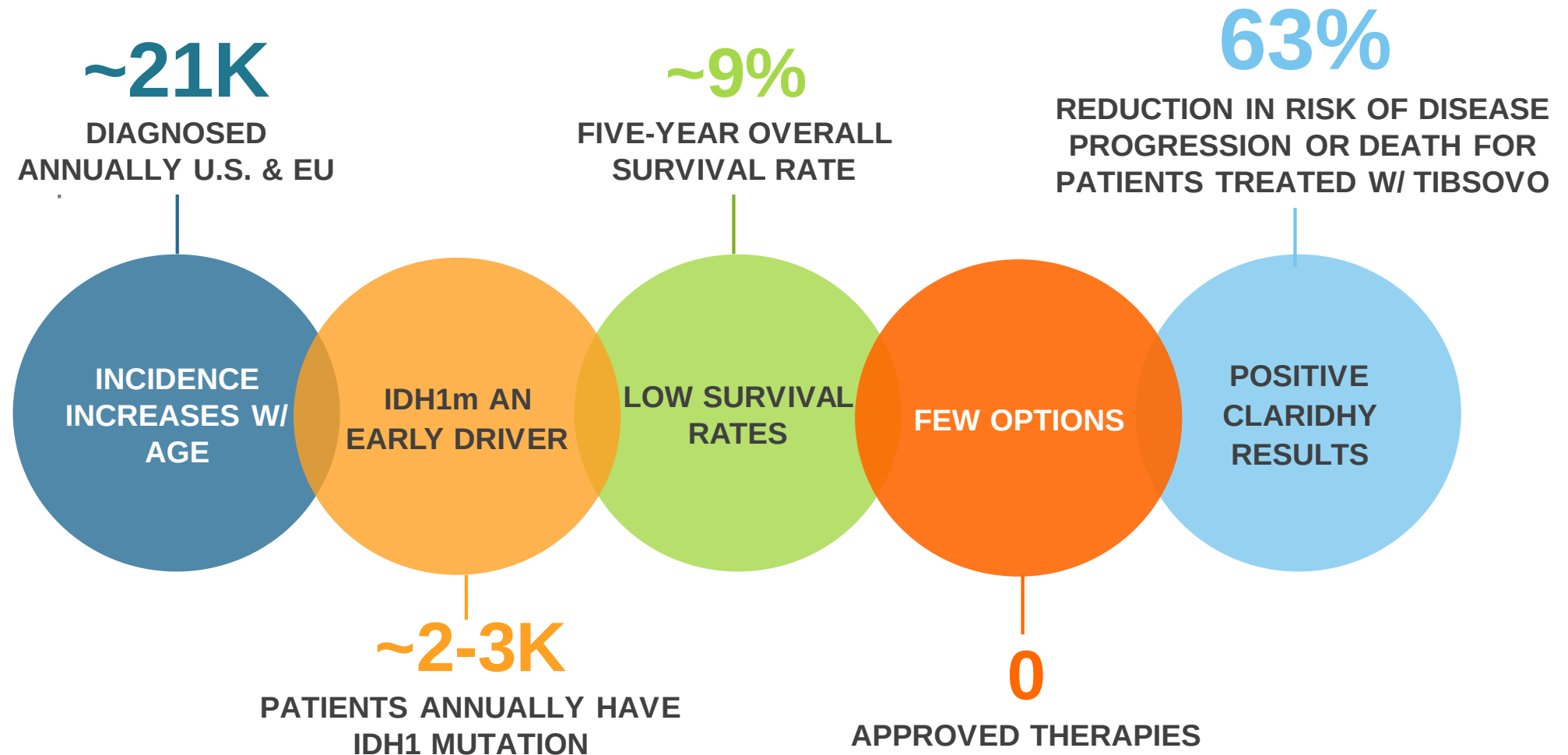
CHOLANGIOCARCINOMA



LOW GRADE GLIOMA



No Approved Targeted Therapies for Second-line or Later Cholangiocarcinoma

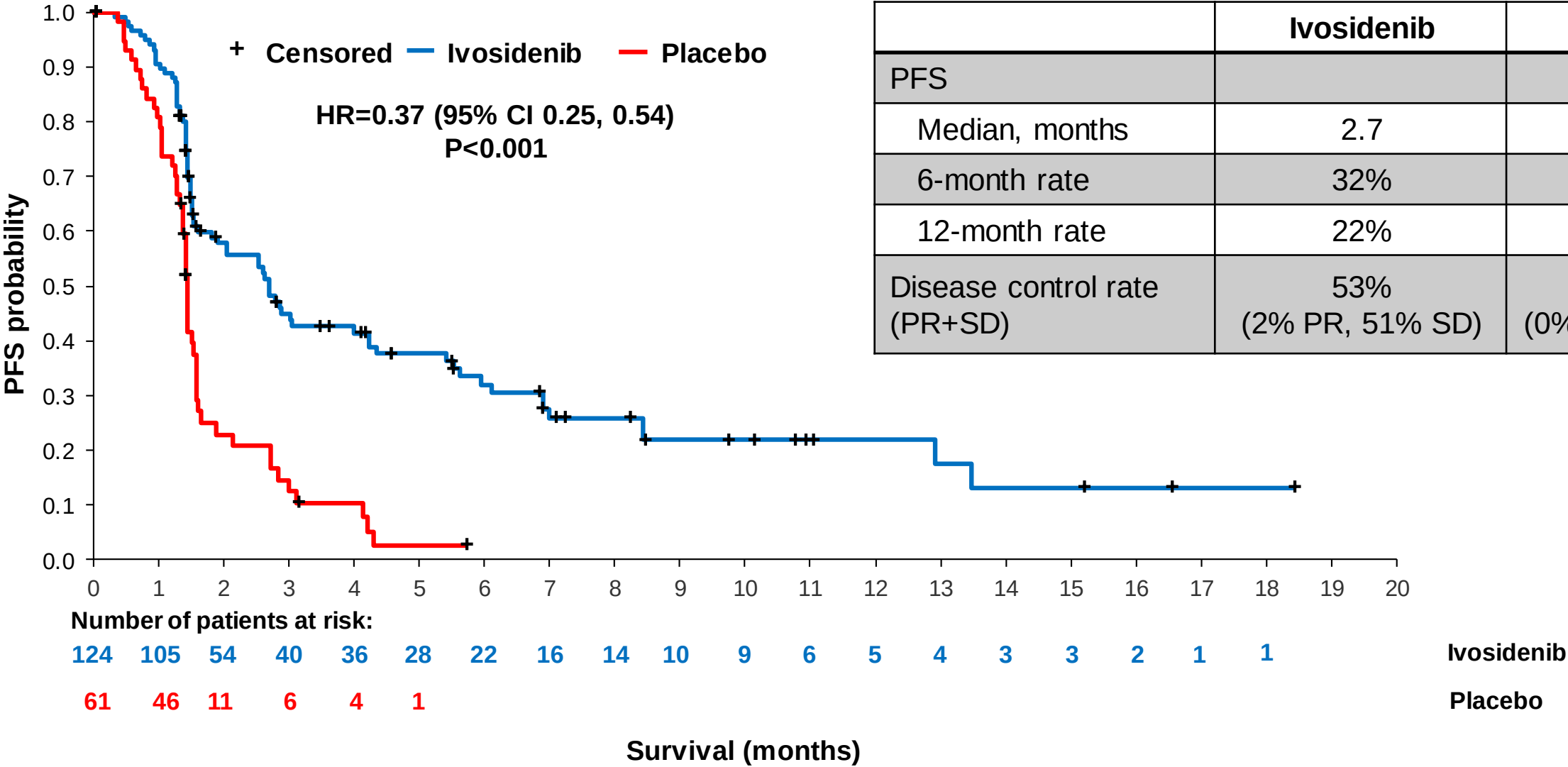


Sources: CDC National Program of Cancer Registries (NPCR); Epiphany Partners Epic Oncology; Decision Resources; Market Research; Borger DR et al. Oncologist 2012;17:72-9.; Kipp BR et al. Hum Pathol 2012;43:1552-8.; Goyal L et al. Oncologist 2015;20:1019-27; data from ESMO 2019



Phase 3 ClarIDHy Study Achieved Primary Endpoint, Demonstrating Statistically Significant Improvement in PFS

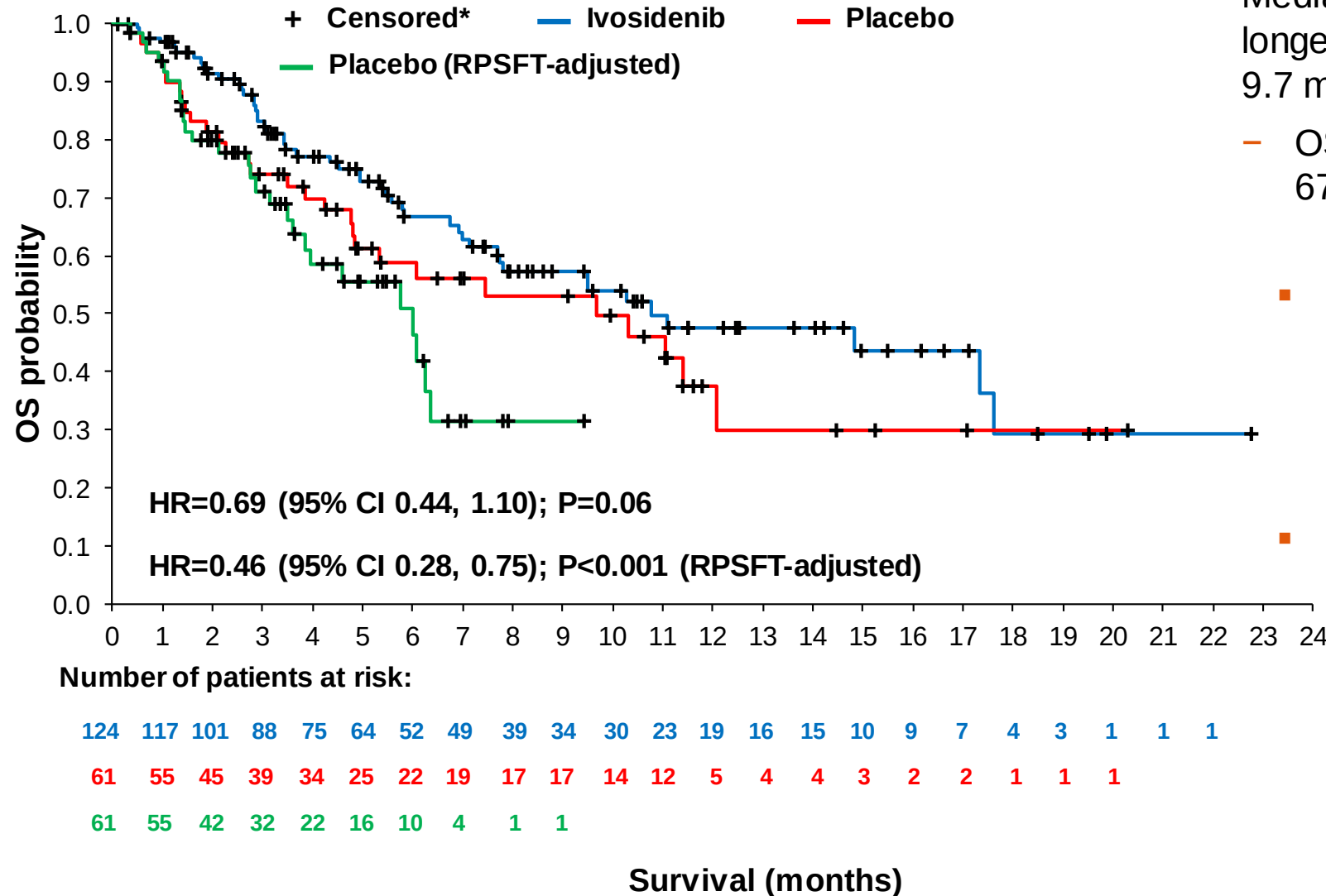
Safety Profile Consistent with Published Phase 1 Data in Patients with IDH1 Mutant Solid Tumors



	Ivosidenib	Placebo
PFS		
Median, months	2.7	1.4
6-month rate	32%	NE
12-month rate	22%	NE
Disease control rate (PR+SD)	53% (2% PR, 51% SD)	28% (0% PR, 28% SD)



Overall Survival Trending Positive with ~50% of Total Events; Statistically Significant When Adjusting for Crossover



- Median OS based on 78 events was numerically longer with ivosidenib than placebo (10.8 vs. 9.7 months)
- OS rates at 6 and 12 months for ivosidenib: 67% and 48% vs. 59% and 38% for placebo
- Rank-preserving structural failure time (RPSFT)^{1,2} method used to reconstruct the survival curve for the placebo subjects as if they had never crossed over to ivosidenib
- With the RPSFT method, the median OS with placebo adjusts to 6 months

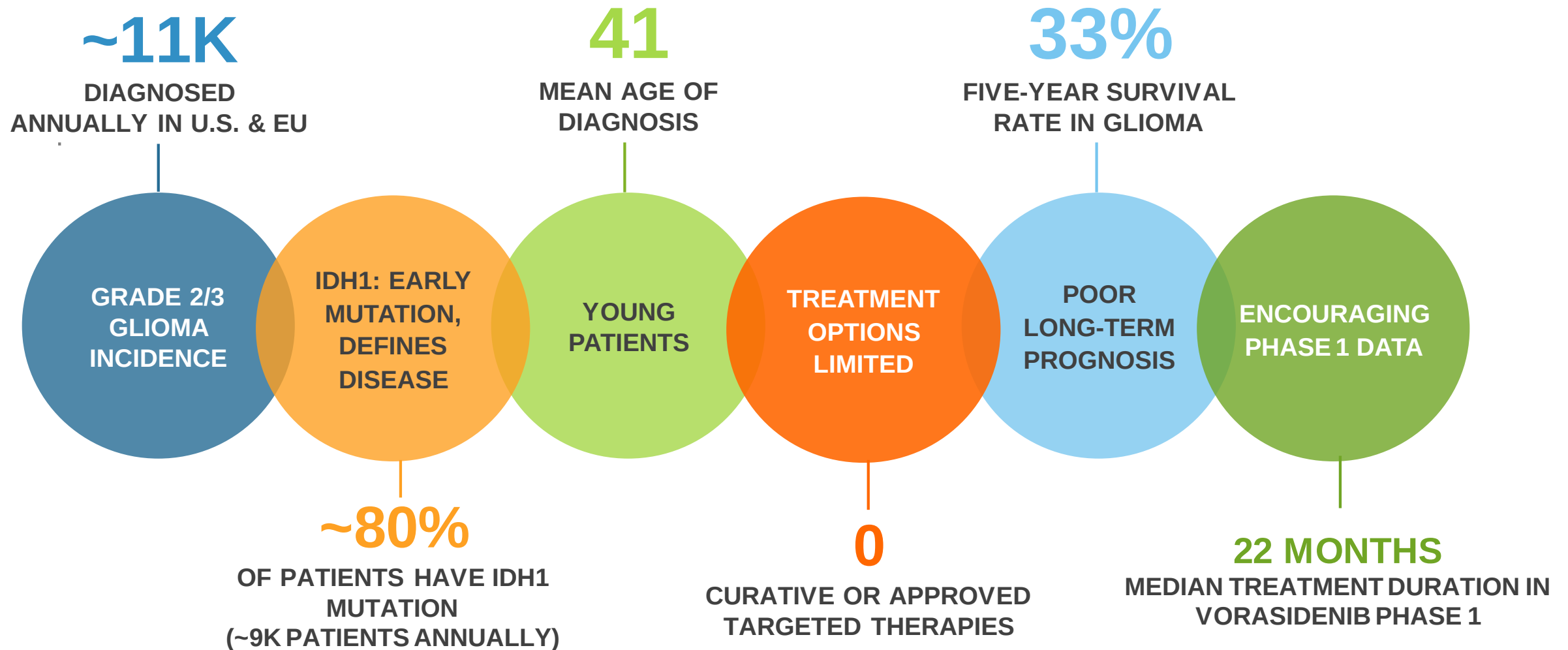
*Patients without documentation of death at the data cutoff date were censored at the date the patient was last known to be alive or the data cutoff date, whichever was earlier.

20 1. Watkins C, et al. *Pharm Stat*. 2013;12:348-357. 2. Robins JM, Tsiatis AA. *Commun Stat Theory Methods*. 1991;20:2609-2631.

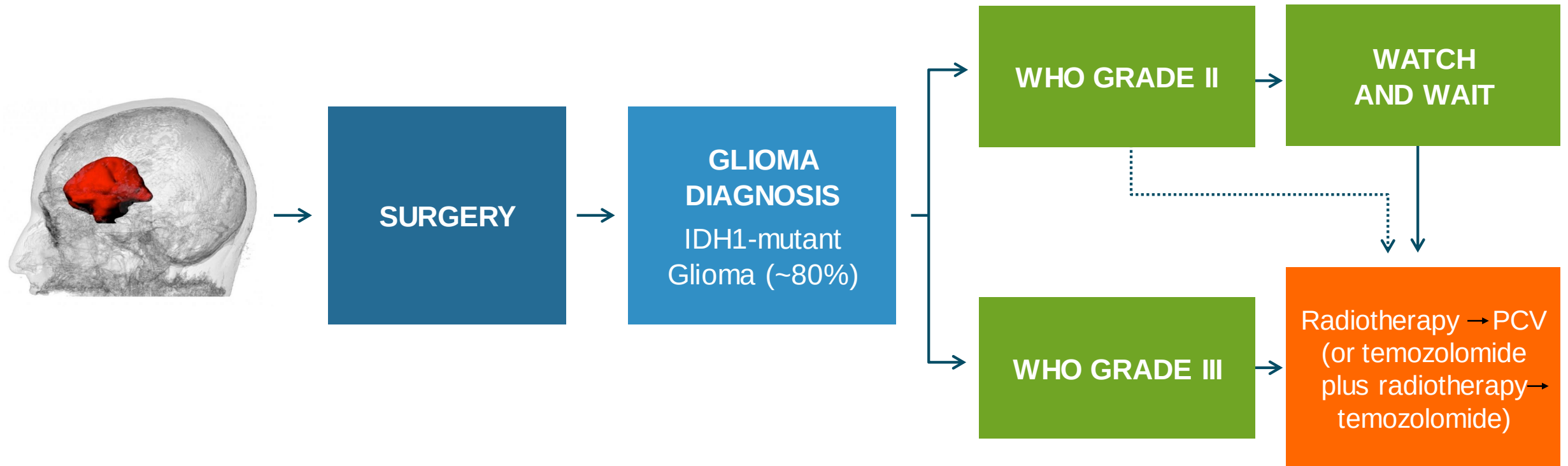
Data presented at ESMO 2019



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



Current Treatment Paradigm for IDHm Gliomas



Global Phase 3 INDIGO Study of Vorasidenib in IDH Mutant Low-Grade Glioma



Key Eligibility Criteria

- ≥ 12 years of age
- IDH-mutated Grade 2 oligodendroglioma or astrocytoma per WHO 2016
- Prior surgery only
- Measurable residual or recurrent disease

1:1 double-blind randomization (n=366)

Stratified by 1p19q status and baseline tumor size

Vorasidenib
50 mg QD orally
Continuous 28-day cycles
(n=183)

Matched placebo*
(n=183)

**centrally-confirmed progressive disease will permit unblinding and crossover*

Endpoints

Primary: Progression free survival (by BIRC)

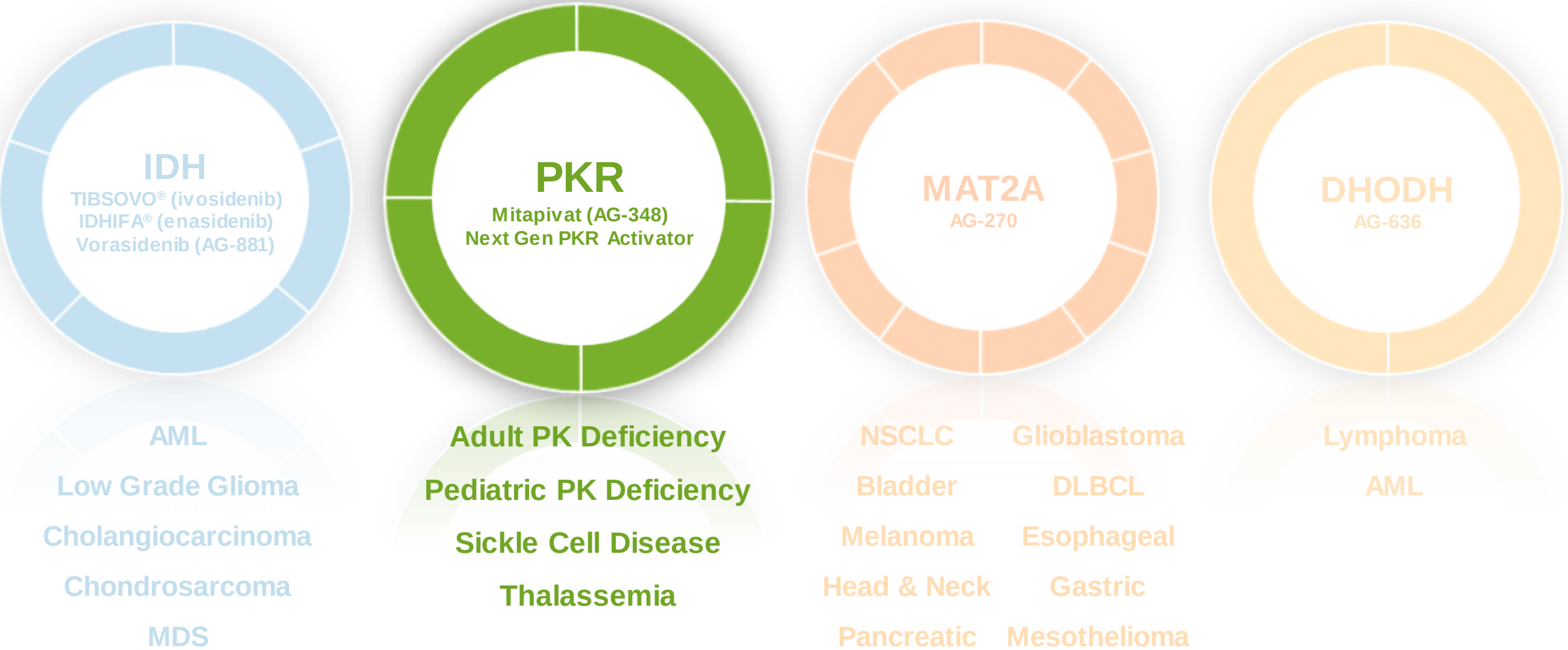
Secondary/Exploratory: Tumor volume, safety, ORR, OS, QOL, seizures, neuro-cognitive function, time to next intervention

BIRC = blinded independent review committee, ORR = overall response rate, OS = overall survival, QOL = quality of life, WHO = World Health Organization

Registration-enabling study on track to initiate by year-end 2019



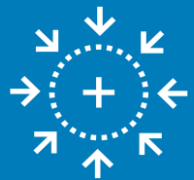
Productive Research & Discovery Engine Has Produced
Four Key Targets with Multiple Disease Opportunities



Our Approach to Rare Genetic Diseases

Part of a New Wave of Potentially Transformational Therapies

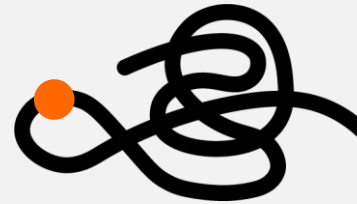
Understanding and correcting the root cause of the disease



AGIOS APPROACH →

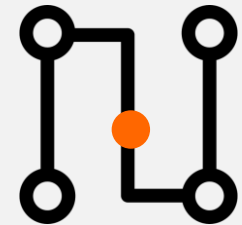
Disease-modifying small molecules targeting intracellular pathways leading to potentially transformative outcomes for patients

Mutated metabolic enzyme



Biochemical defects

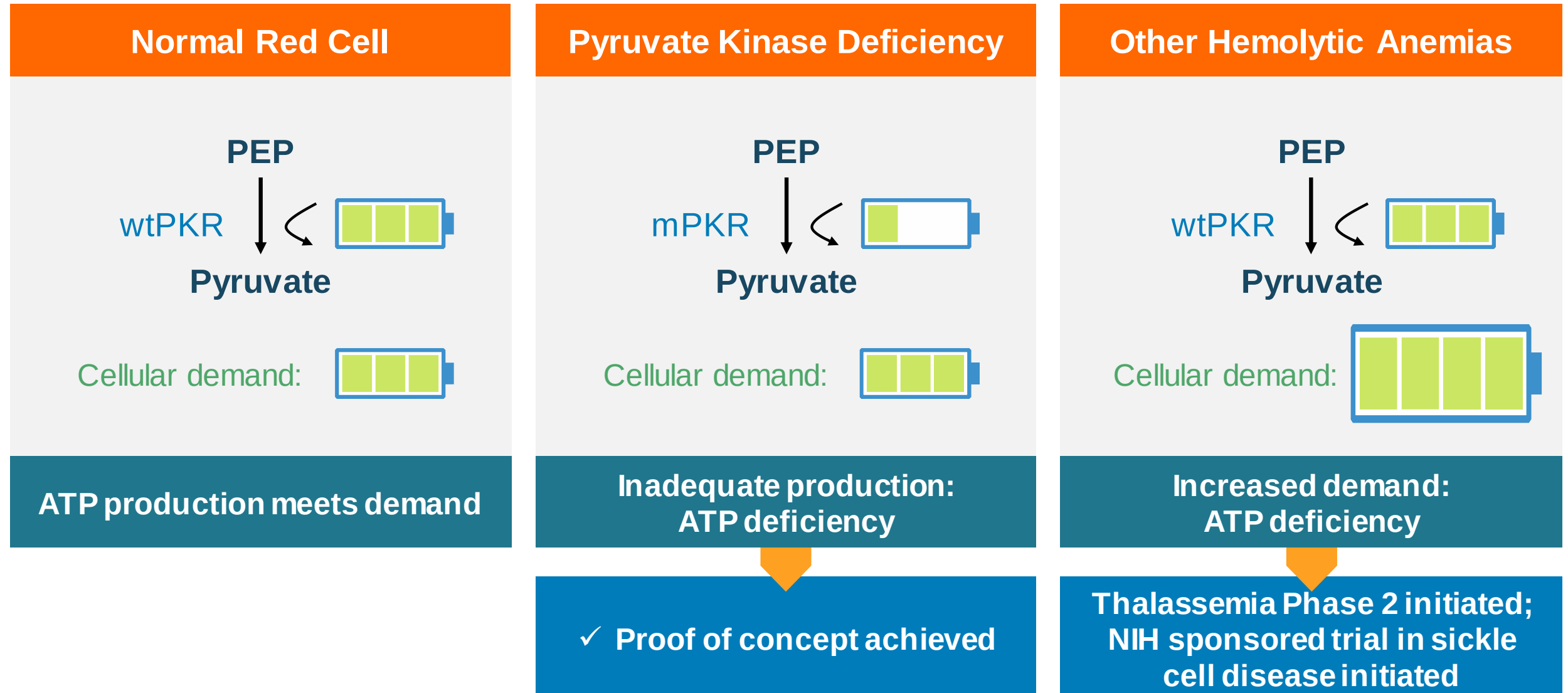
Disrupted metabolic networks



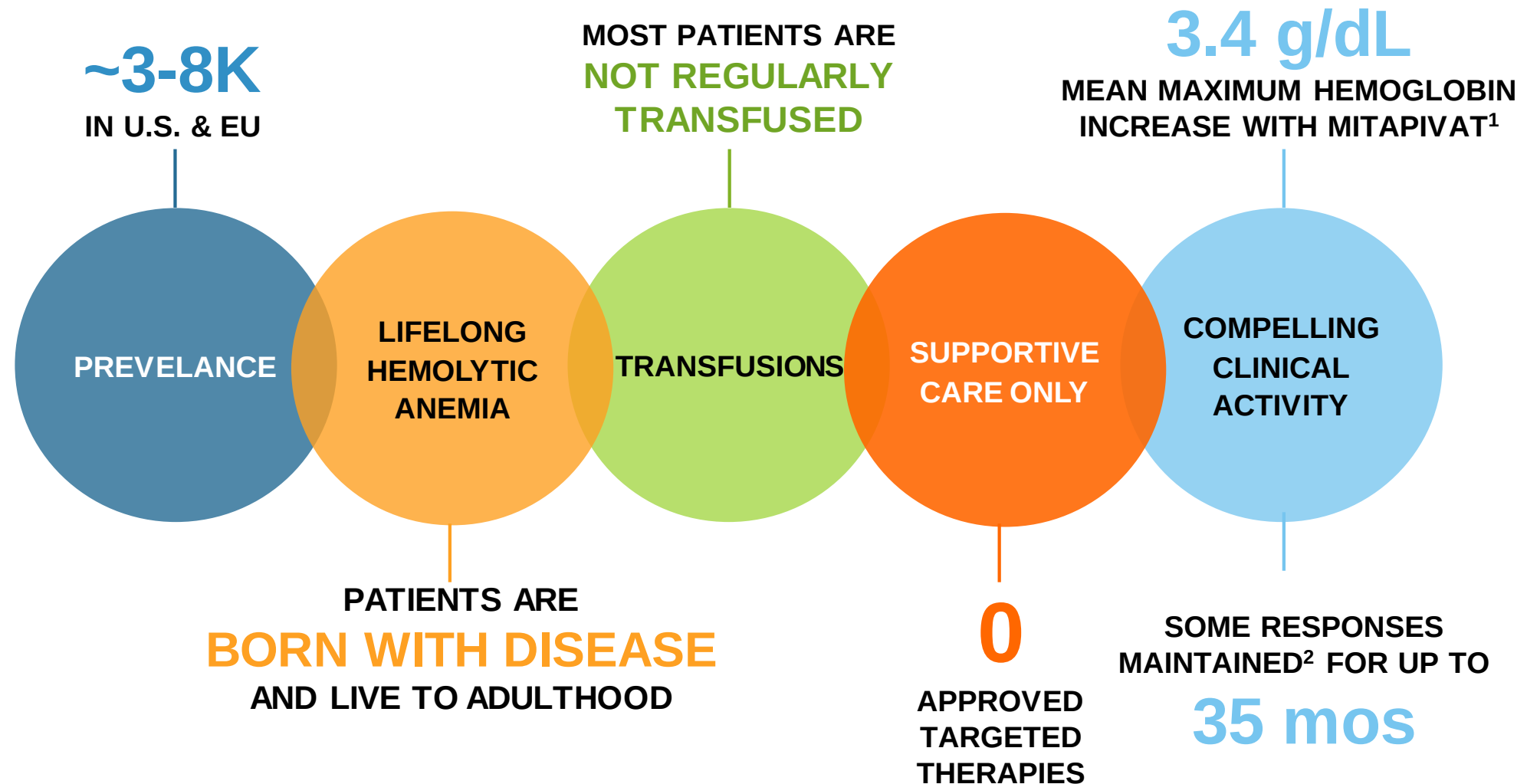
Toxic or deficient metabolites



PK Activation Represents Opportunities Across Hemolytic Anemias



Opportunity for Mitapivat to be the First Disease-Modifying Treatment for PK Deficiency



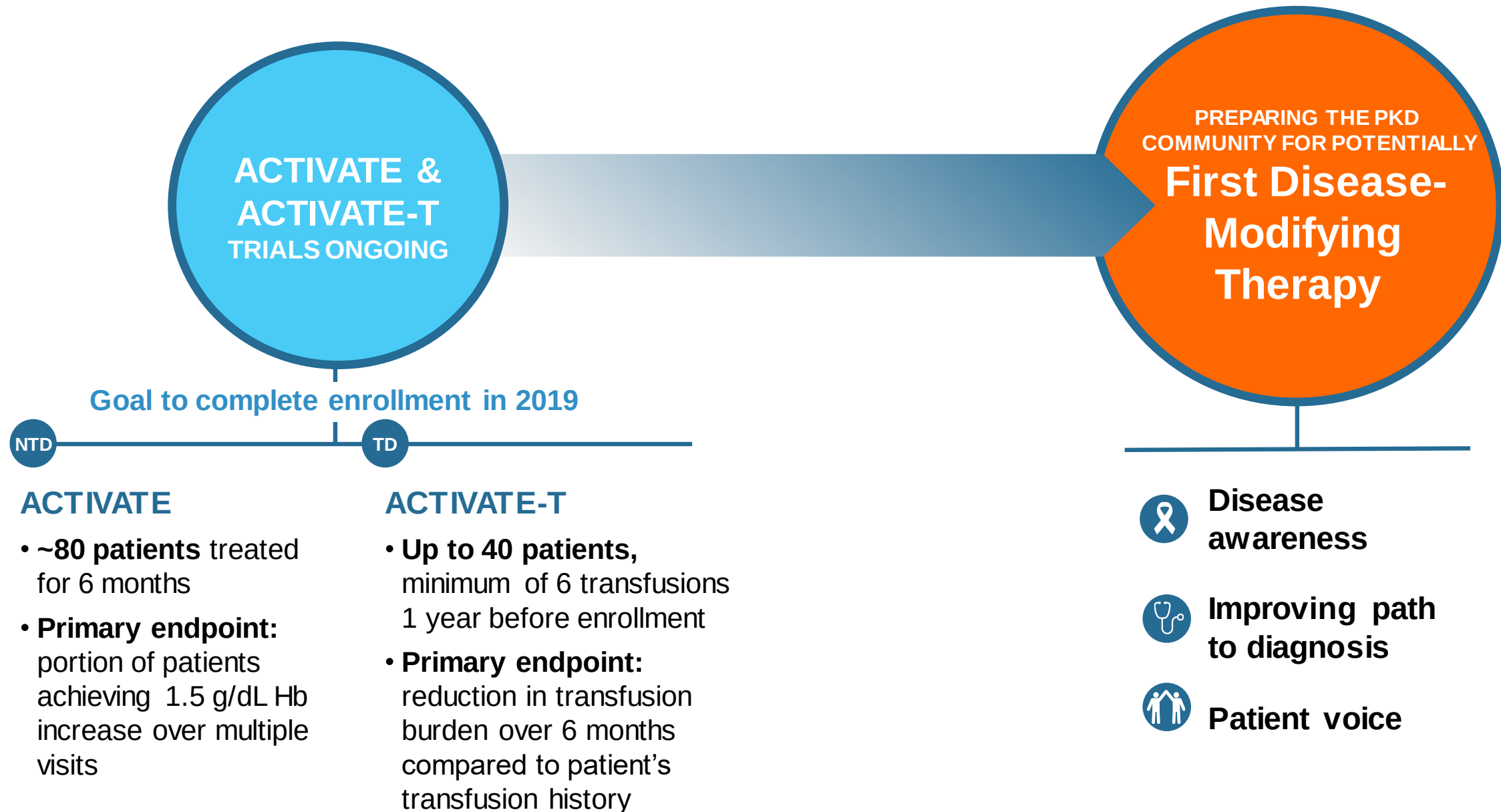
Sources: Estimated prevalence range from ~1:20K to ~1:485K Grace R et al. *Am J Hematol* 2015;90(9):825-30; ¹Mohrenweiser HW *PNAS* 1981;78(8):5046-50; ²Carey PJ et al. *Blood* 2000;96(12):4005-6; ³Beutler E & Gelbart T *Blood* 2000;95(11):3585-8; ⁴deMedicis et al. *Hum Hered* 1992;42(3):179-83; Grace R et al. *N Engl J Med* 2019;381:933-44

¹Mean maximum hemoglobin increase of 3.4 g/dL in patients to had a >1.0 g/dL increase in haemoglobin on study; ² 19 pts remain in the extension phase with a median treatment duration of 28.9 months [range 21.6-34.8]

New data from the extension phase of the Phase 2 DRIVE PK study of mitapivat in adults with PK deficiency accepted for presentation at ASH



Mitapivat Path to Approval



Broadening the Opportunity for Mitapivat in Thalassemia and Sickle Cell Disease



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

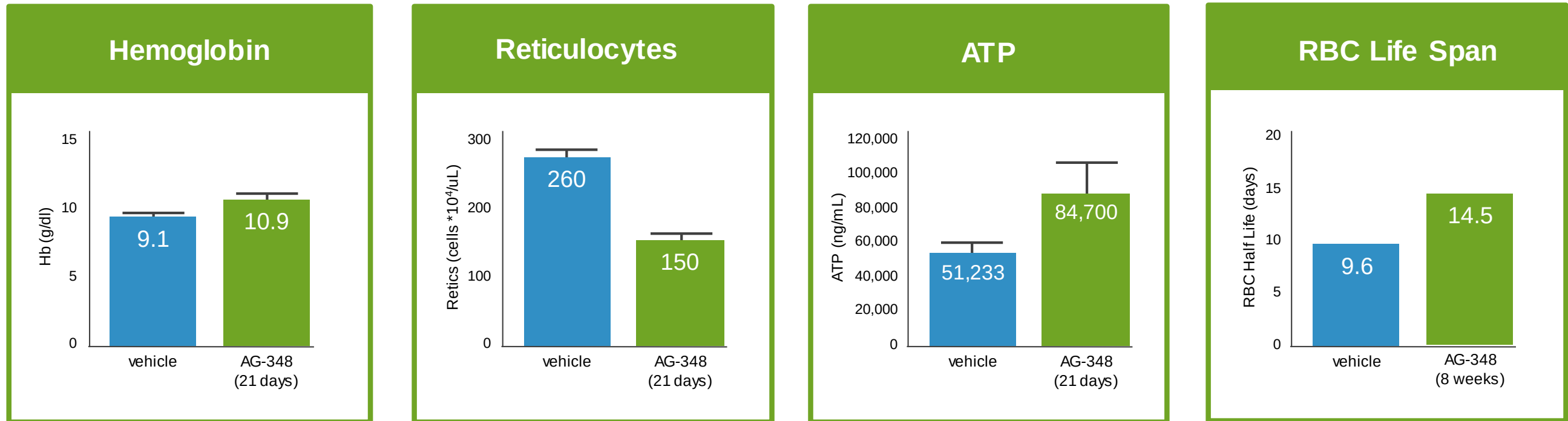


NIH STUDY IN SICKLE CELL DISEASE ENROLLING

- ~25 adults with sickle cell disease
- Evaluating 5, 20 and 50 mg BID
- Primary endpoints: safety, tolerability and changes in laboratory parameters, including hemoglobin levels
- Study conducted as part of Cooperative Research and Development Agreement with Dr. Swee Lay Thein at the NIH



Mitapivat Improves Red Cell Parameters in a Beta-thalassemia Mouse Model



- Treatment with mitapivat for up to 2 months shows sustained improvement in hematological parameters
- Sharp reduction in circulating immature red cells suggests amelioration of ineffective erythropoiesis
- ~50% increase in lifespan of peripheral RBCs

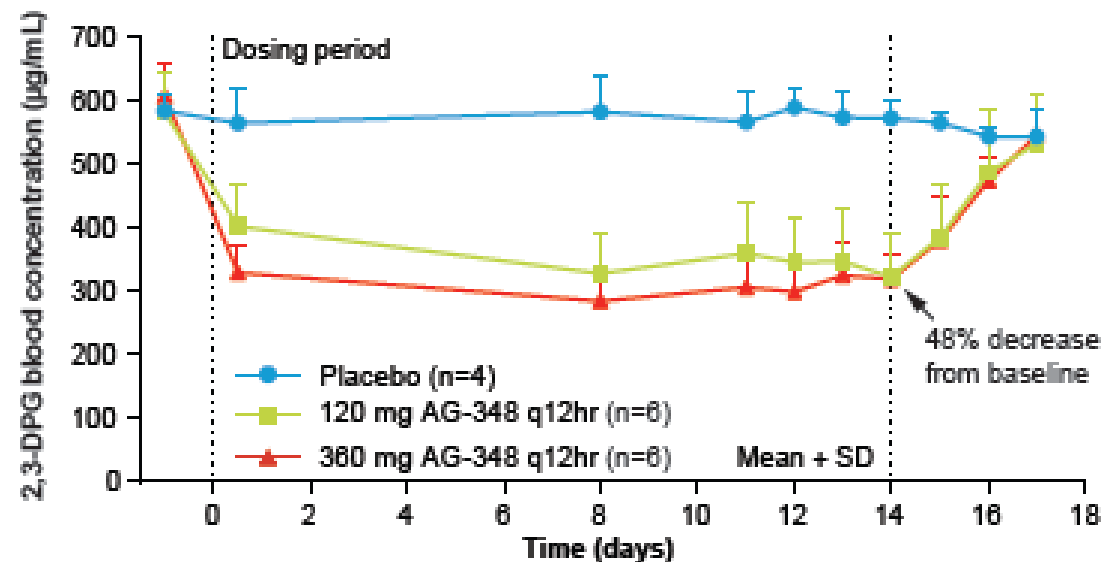
■ Vehicle
■ Mitapivat (AG-348)
(Hb, reticulocytes & ATP, 21 days RBC half life, 8 weeks)



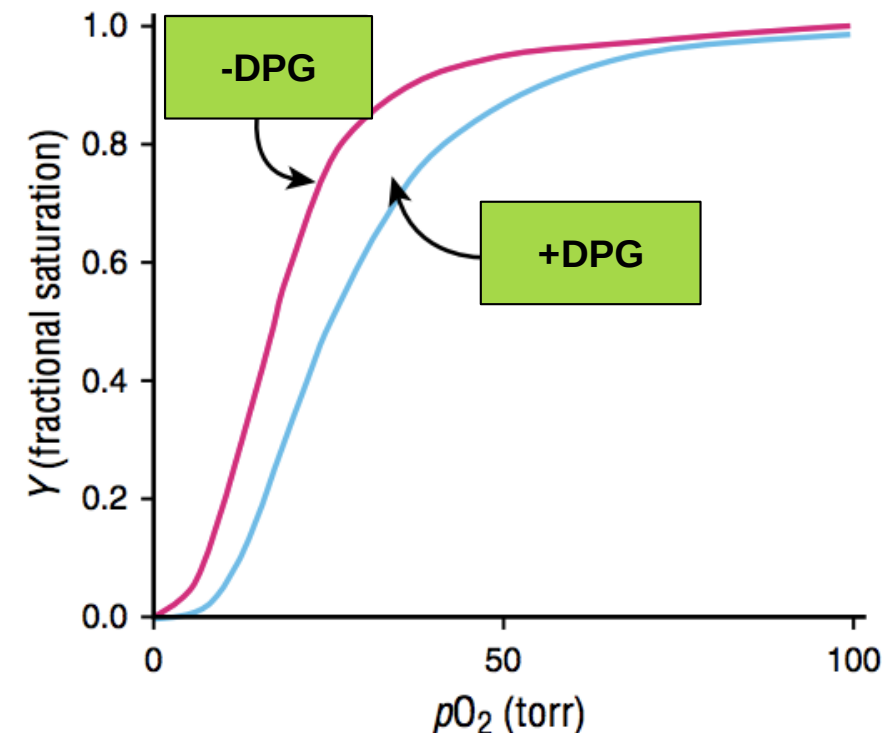
Therapeutic Hypothesis for AG-348: Modulation of 2,3-DPG and ATP Levels Will Reduce HbS Polymerization

Activation of WT PKR in healthy volunteer clinical studies shows ~50% reduction in 2,3-DPG

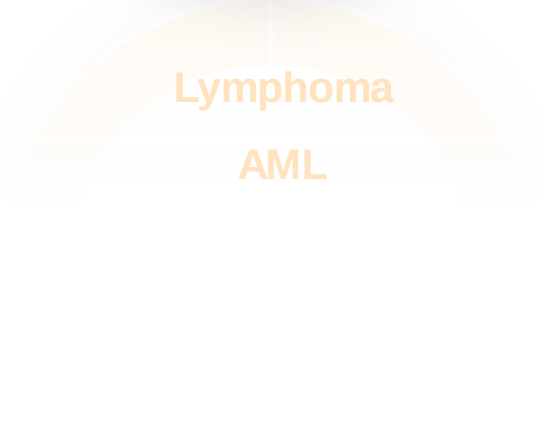
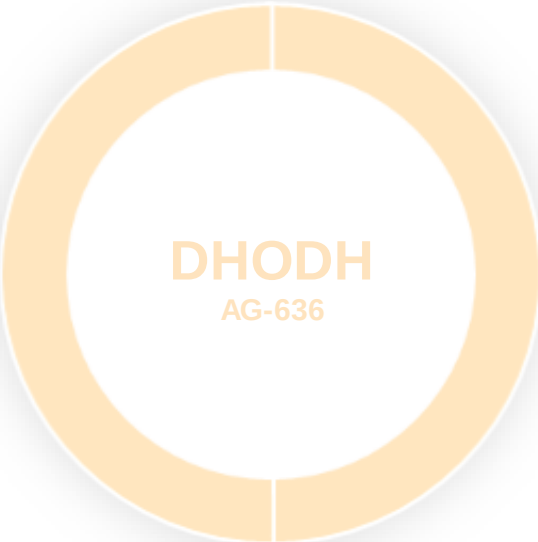
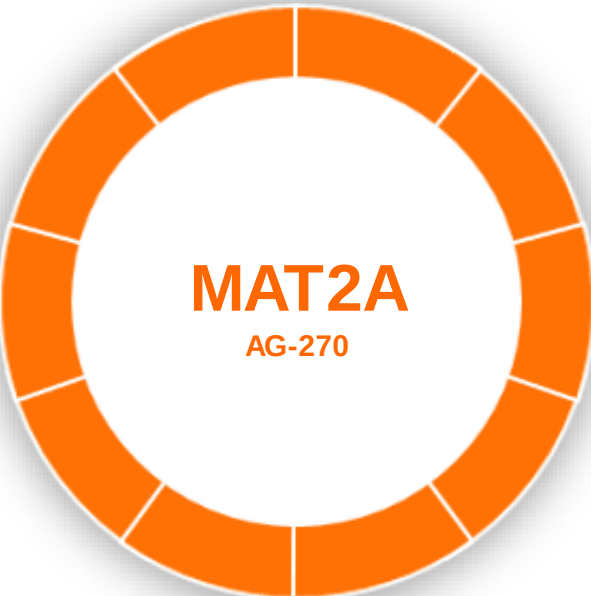
Mean blood concentration-time profiles of 2,3-DPG following multiple oral doses of AG-348 (cohorts 1 and 2 only)



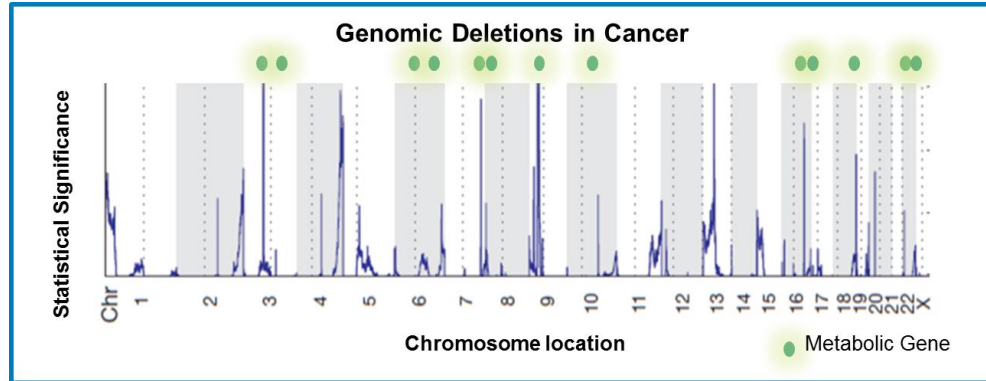
DPG depletion shifts T to R



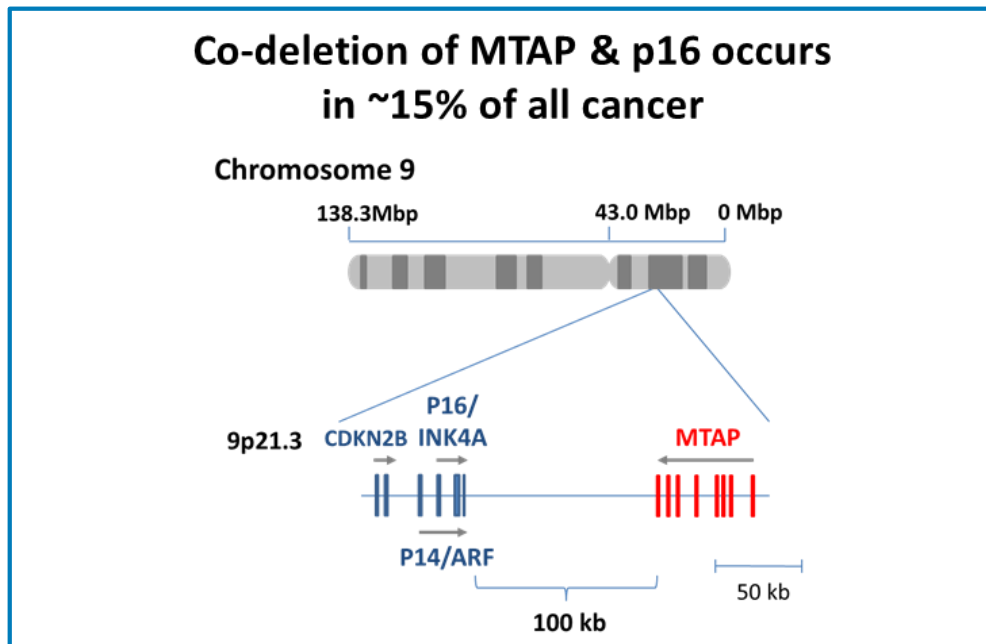
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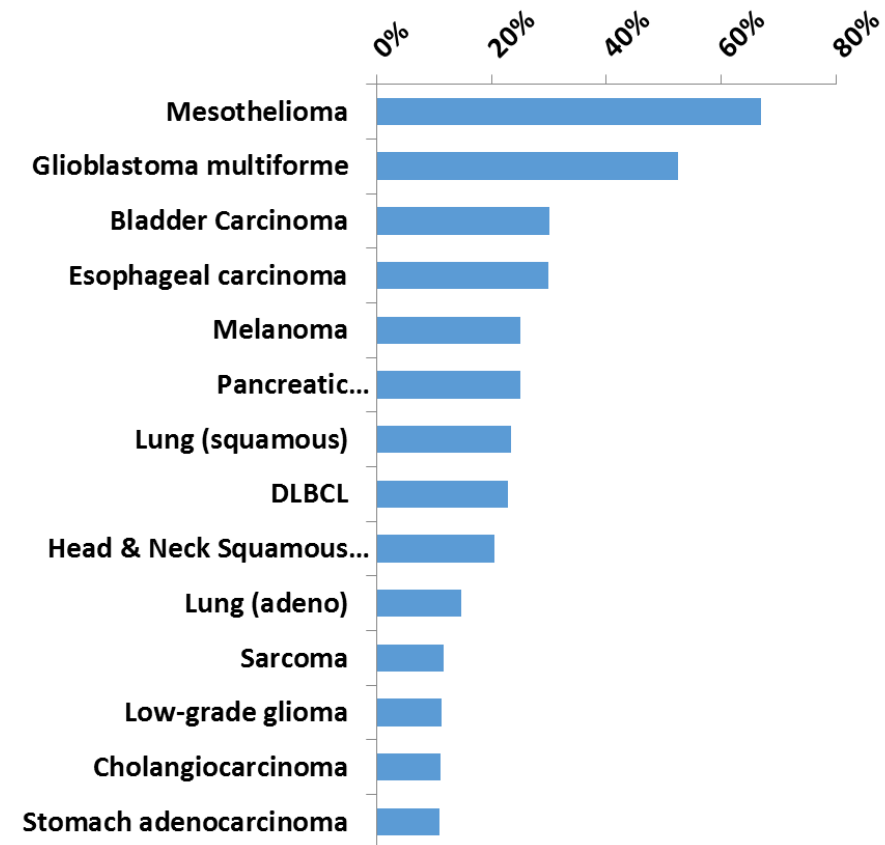
MTAP Deletions Occur in ~15% of All Cancers



Source: Adapted from Beroukhim et al Nature 2010

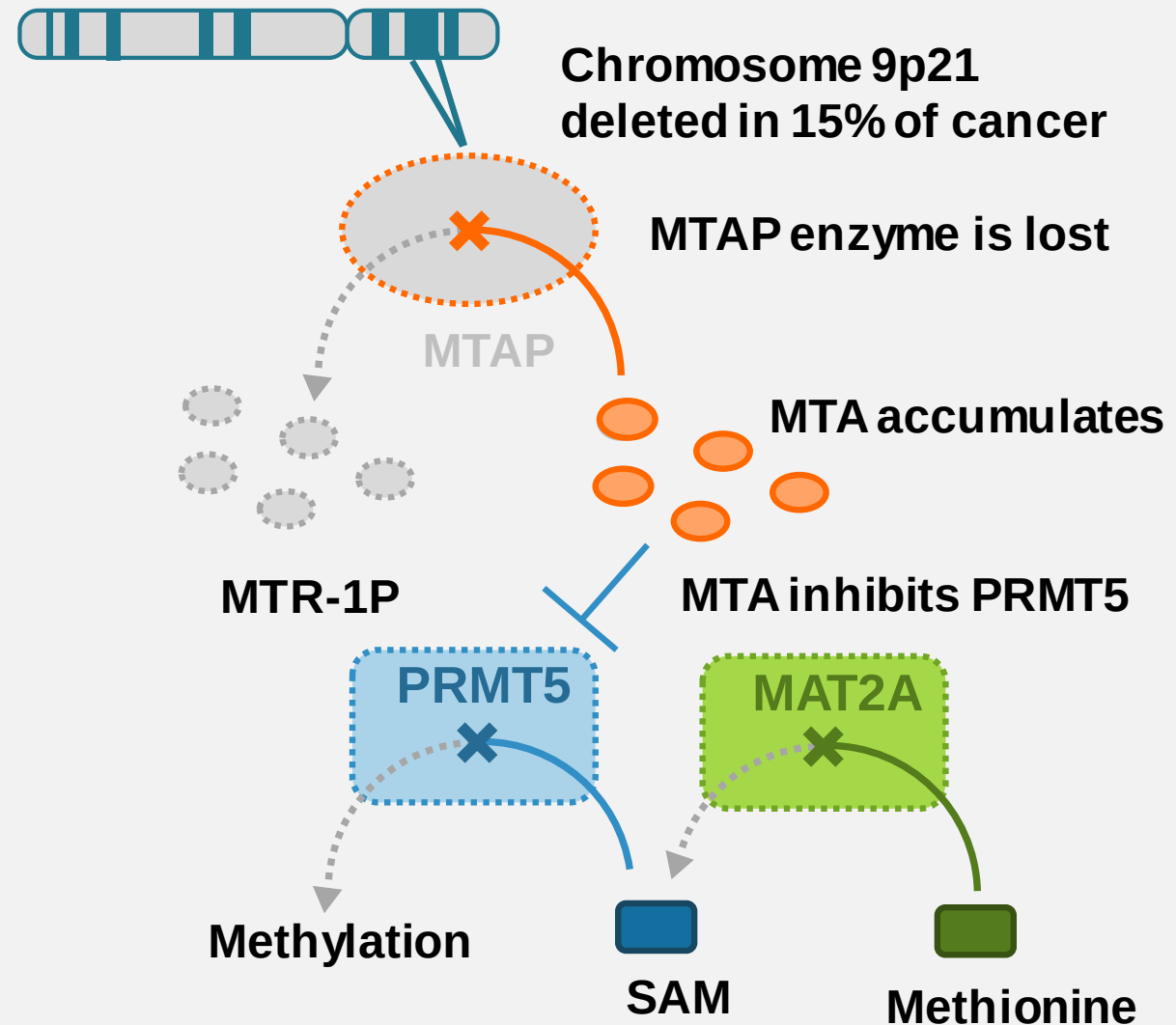


MTAP Deletion Frequency

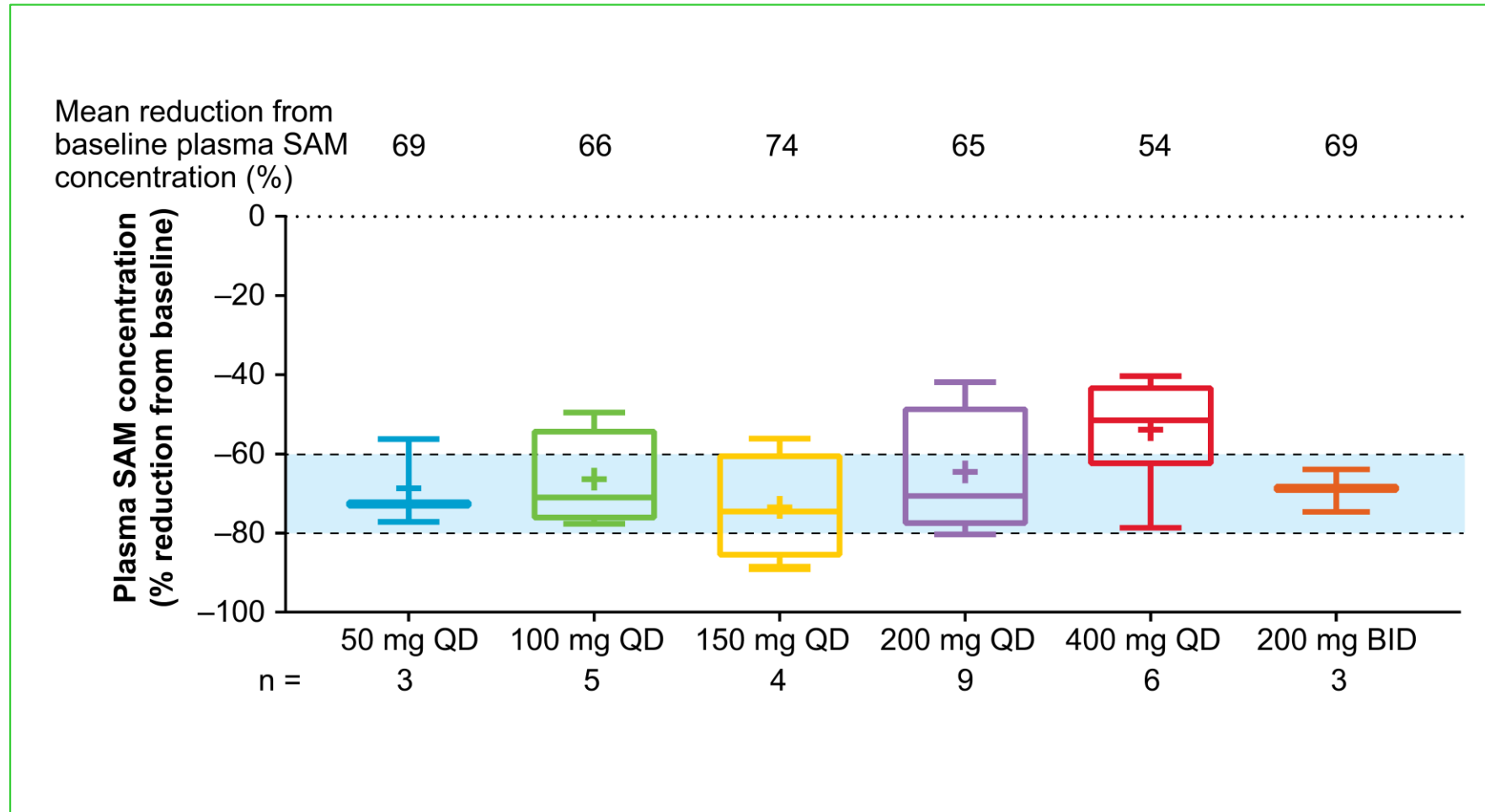


A Key Insight: Deletion of MTAP Makes Cancers Vulnerable to Targeting of MAT2A

- 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



AG-270 Achieves Targeted Reductions in SAM in Range Associated with Preclinical Maximum Tumor Growth Inhibition

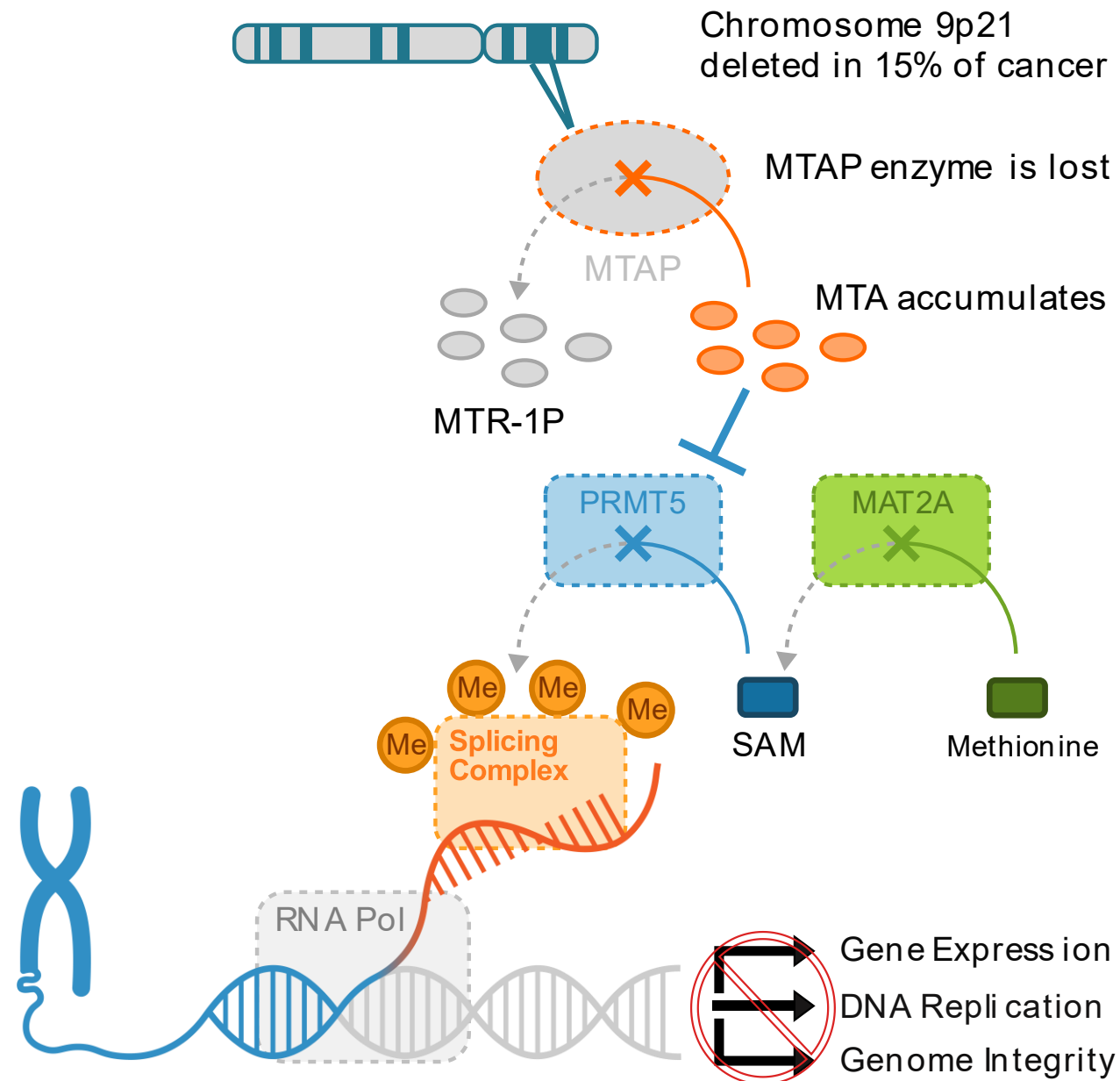


Box denotes 25th to 75th percentiles, horizontal bar the median, and + the mean, with whiskers extending to the minimum and maximum values

- Plasma SAM concentration at C1D15 decreased by 65–74% across doses of 50–200 mg QD and 200 mg BID
- The lower reduction in plasma SAM concentration (~54%) observed at 400 mg QD is consistent with the lower AG-270 exposure observed at this dose
- Average reductions in plasma SAM concentration are within the range associated with maximum tumor growth inhibition in preclinical models (60–80%)



MAT2A Inhibition Leads to DNA Damage and Cell Cycle Defects, Leading to Strong Synergy with Anti-mitotic Taxanes



AG-270 Advancing to Next Phase of Clinical Development

SINGLE AGENT PHASE 1 DOSE-ESCALATION COMPLETE

39 treatment-refractory
advanced solid tumors
or lymphoma patients
with MTAP/CDKN2A
deletion



- ✓ AG-270 generates reductions in plasma SAM concentration and in levels of tumor SDMA at well-tolerated doses
- ✓ Safety profile well characterized
- ✓ MTD determined to be 200 mg QD

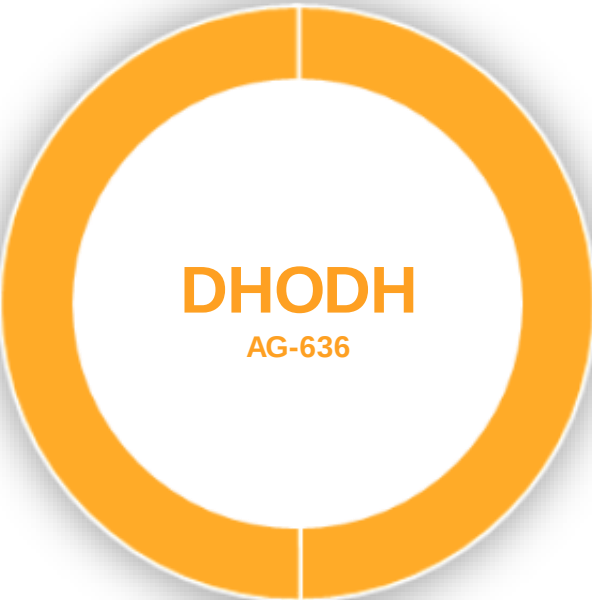
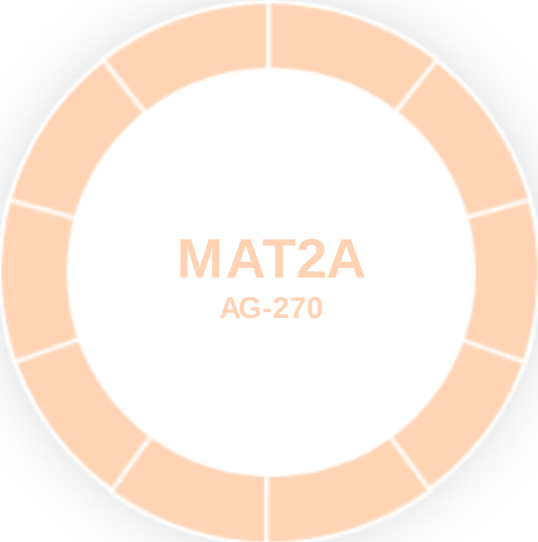
COMBINATION ARMS INITIATED

AG-270 + docetaxel in
MTAP-deleted NSCLC (2nd line)
N = up to 40

AG-270 + nab-paclitaxel and
gemcitabine in MTAP-
deleted pancreatic ductal
adenocarcinoma (1st or 2nd line)
N = up to 45



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Four Key Targets with Multiple Disease Opportunities



Phase 1 Study of DHODH Inhibitor AG-636 in Lymphoma

DHODH catalyzes a critical step in pyrimidine biosynthesis

Dihydroorotate



Orotate



UMP



RNA/DNA biosynthesis

LYMPHOMA

Phase 1 Study in Treatment Refractory Lymphoma Ongoing

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



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



Third Quarter 2019 Financial Results

Statement of Operations	Three Months Ended 9/30/19	Three Months Ended 9/30/18
Total Revenue	\$26.0M	\$15.2M
Collaboration Revenue	5.9M	8.7M
TIBSOVO® Net Sales	17.4M	4.5M
Royalty Revenue	2.7M	2.0M
Cost of Sales	0.4M	0.7M
Research & Development Expense	101.7M	82.6M
Selling, General & Administrative Expense	33.0M	31.1M

Balance Sheet	9/30/19	12/31/18
Cash, Cash Equivalents and Marketable Securities	\$540.5M	\$805.4M



2019 Key Milestones & Data Presentations Position Agios for Long-term Value Creation



Key 2019 Milestones

- ✓ FDA approval and commercialization of monotherapy TIBSOVO® in untreated AML
- ✓ Initiate AG-636 Phase 1 dose-escalation trial in lymphoma in 1H 2019
- ✓ Complete AG-270 Phase 1 dose-escalation and select go forward dose
- ✓ Initiate expansion arms in the AG-270 Phase 1 study in Q3 2019
 - Achieve proof-of-concept for mitapivat in thalassemia in 2H 2019
 - Initiate glioma registration-enabling trial with vorasidenib by YE
 - Complete enrollment in PK deficiency pivotal trials ACTIVATE-T and ACTIVATE by YE



Key Upcoming Data Presentations

- Updated data from the perioperative study of ivosidenib and vorasidenib accepted for presentation at the SNO Annual Meeting
- Data from IDH and PKR programs have been accepted for presentation at ASH, including:
 - New data from the extension phase of the Phase 2 DRIVE PK study of mitapivat in adults with PK deficiency
 - Important translational data from the Phase 1 study of TIBSOVO® and azacitidine in frontline AML

