



AgiOS Investor Presentation

June 2019

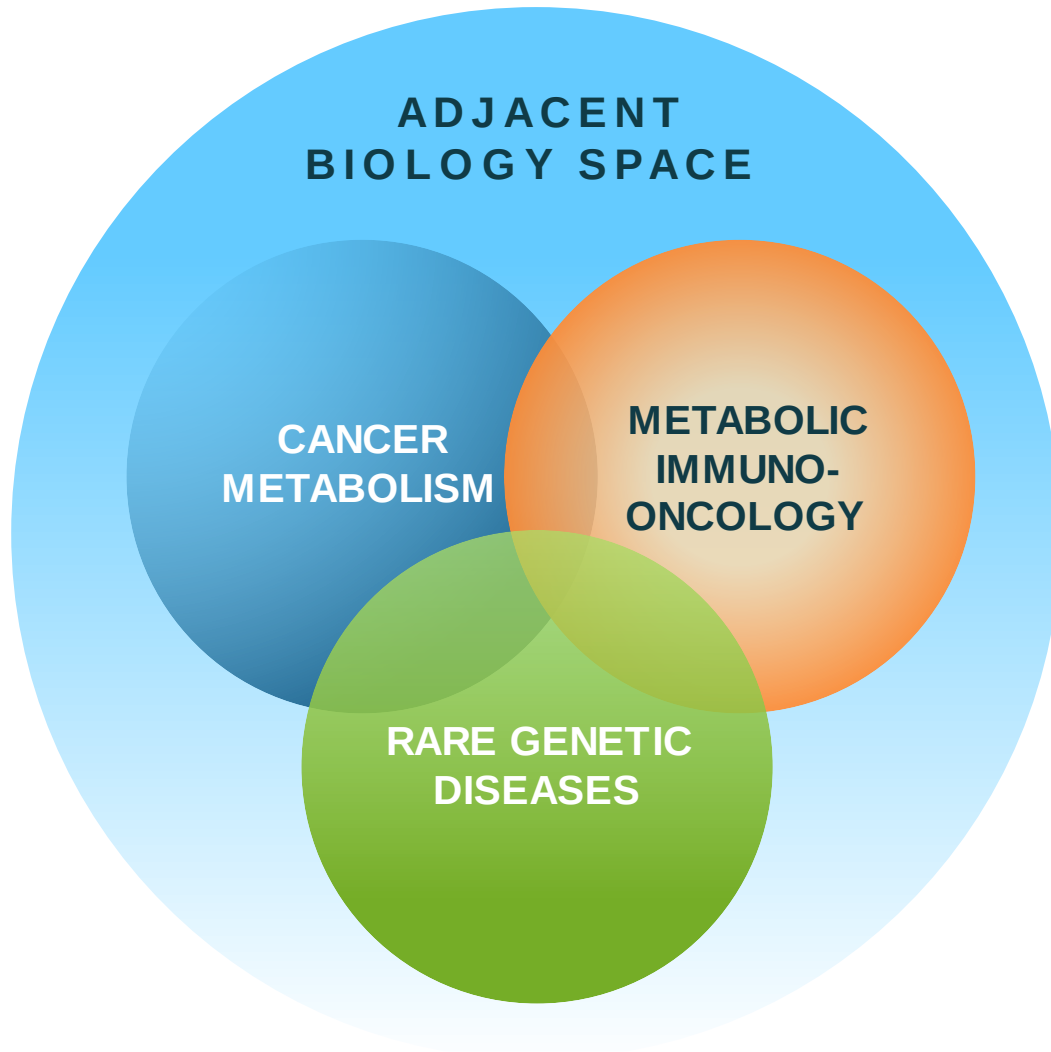


Forward Looking Statements

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," "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.



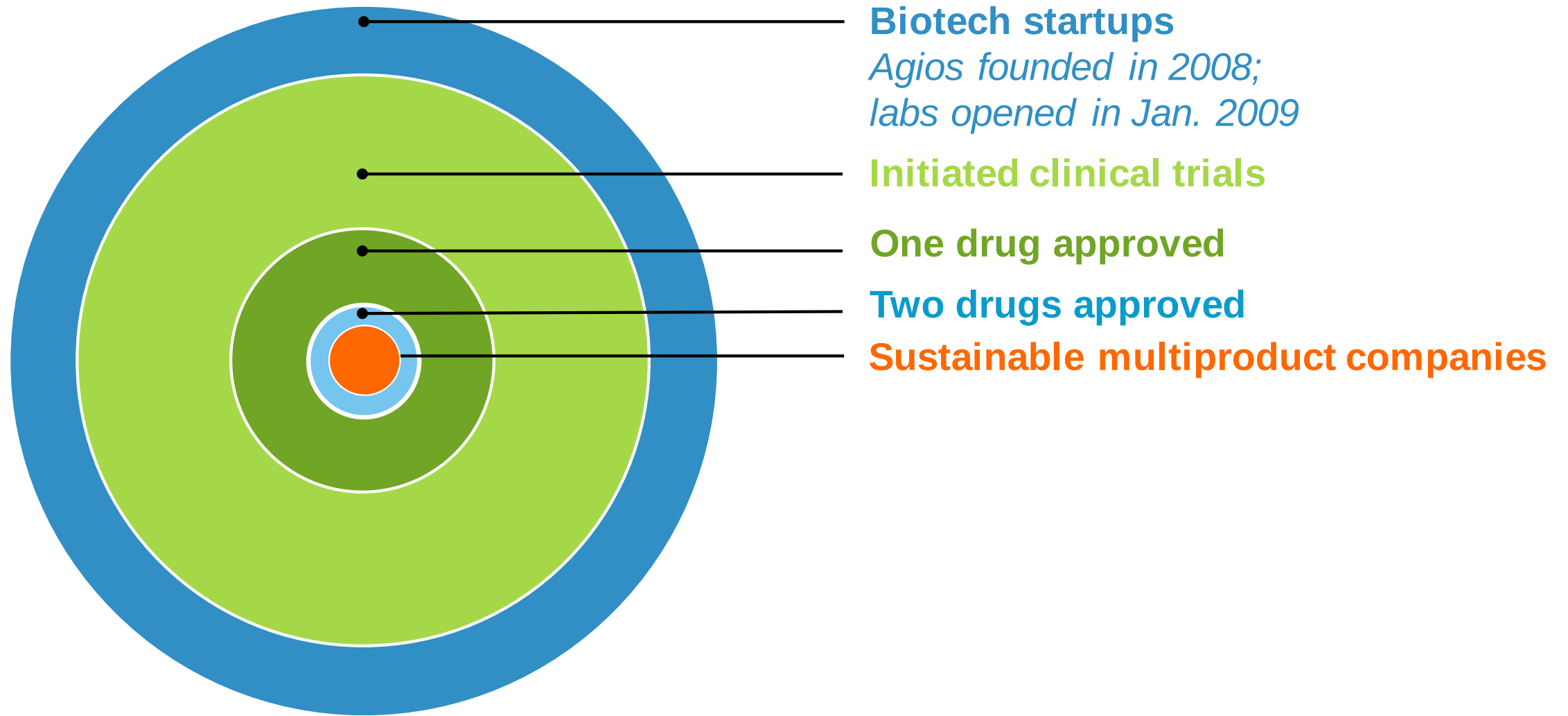
Driven By a Clear Vision and Values



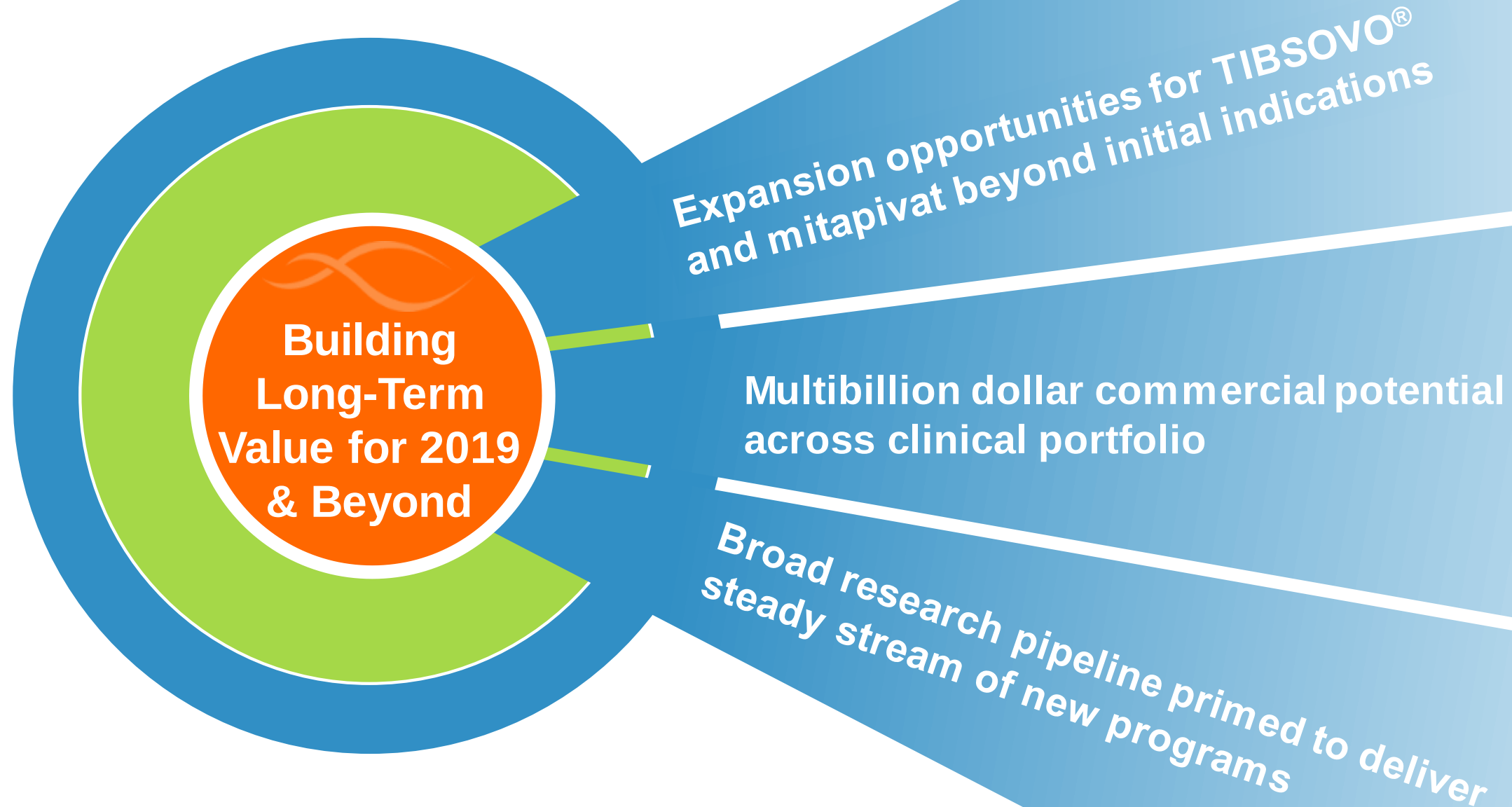
AgiOS is passionately committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and rare genetic diseases.



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

6

DISEASES



5

PIVOTAL CLINICAL TRIALS

8

ADDITIONAL CLINICAL TRIALS



2

MEDICINES
APPROVED

+

4

ADDITIONAL COMPOUNDS
IN CLINICAL DEVELOPMENT

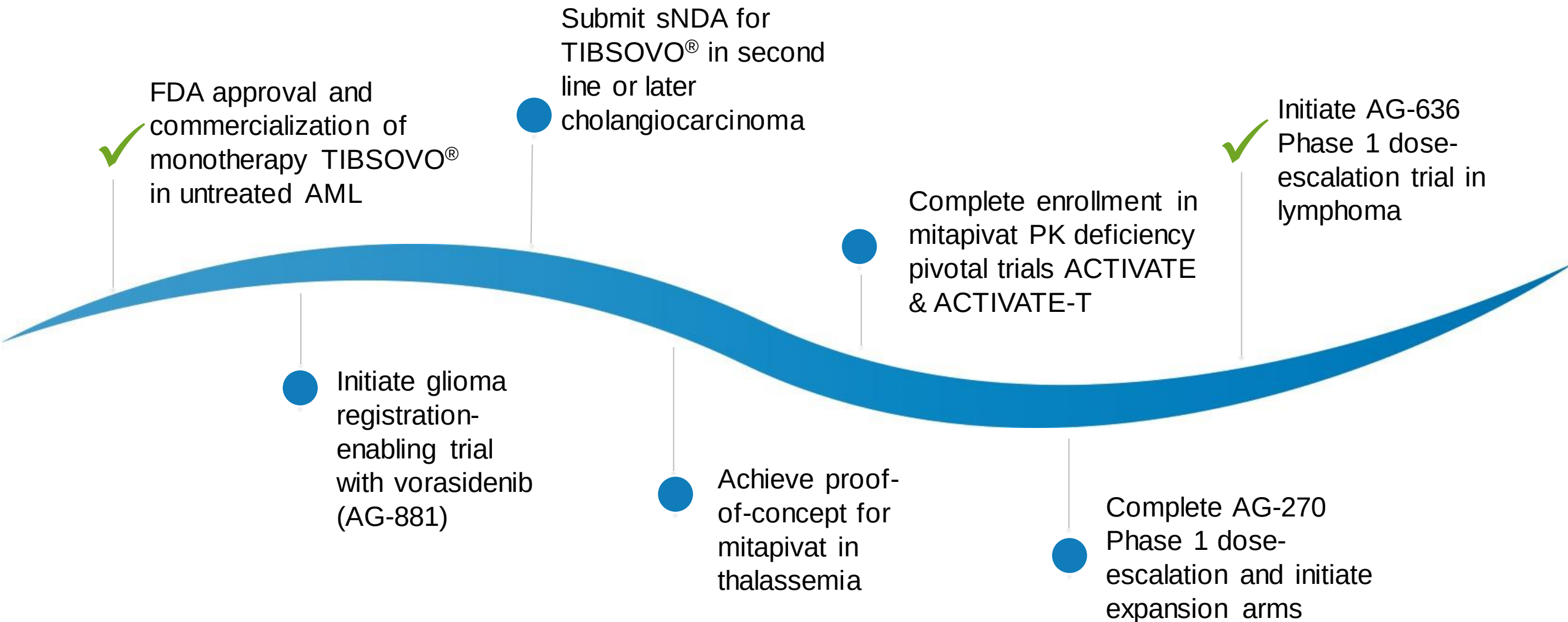


Agios Clinical Pipeline

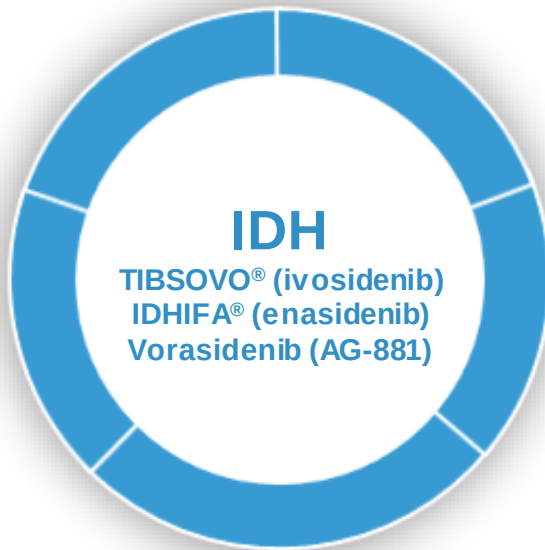
IC = Intensive Chemotherapy

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 (pan-IDHm Inhibitor)	Glioma		Perioperative Study	Phase 3 Study Planned for 4Q 2019			
	Solid Tumors		Phase 1 Dose-Escalation and Expansion				
AG-270 (MTA2A 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



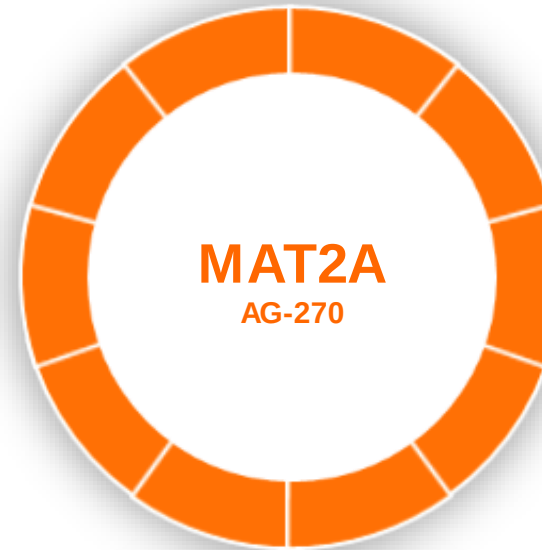
Productive Research & Discovery Engine Has Produced Four Key Targets with Multiple Disease Opportunities



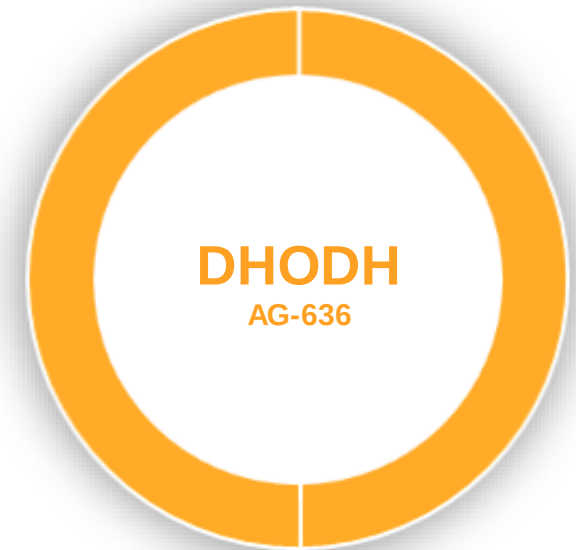
AML
Low Grade Glioma
Cholangiocarcinoma
Chondrosarcoma
MDS



Adult PK Deficiency
Pediatric PK Deficiency
Sickle Cell Disease
Thalassemia



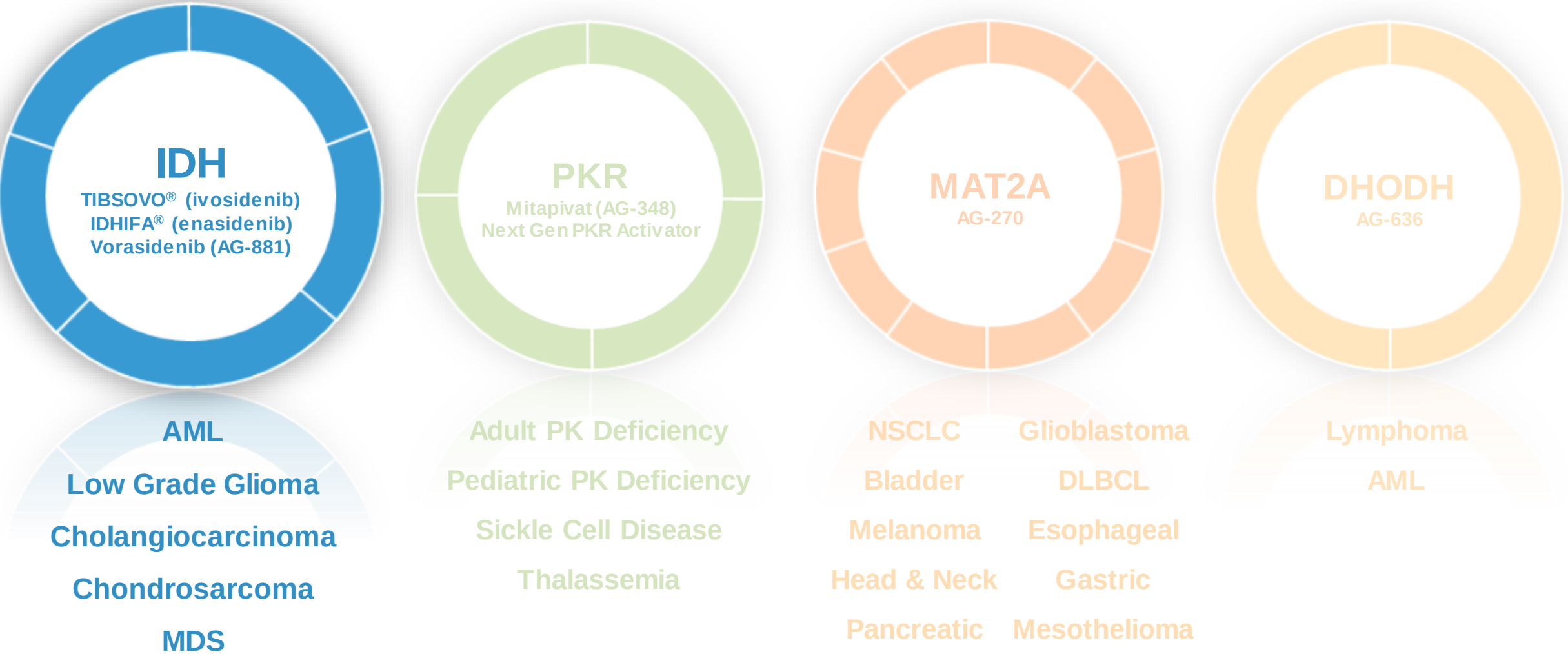
NSCLC Glioblastoma
Bladder DLBCL
Melanoma Esophageal
Head & Neck Gastric
Pancreatic Mesothelioma



Lymphoma
AML



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



What's Possible for IDHm Patients

NOW

- Relapsed/Refractory AML
- Newly diagnosed AML ineligible for intensive chemotherapy

NEXT

- 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



U.S. Co-commercialization
with Celgene



\$9.1M

Q1 2019 U.S. Net Sales



MAA

Submitted & Validated



~90%

Physicians Testing for
IDH1/IDH2 mutations



~15%

Increase in Unique
Prescribers over Q4'18



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%

Intensive Therapy ~60-70%

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

Non-Intensive Therapy ~30-40%

Eligible for
Combination Therapy

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

Not Eligible for
Combination Therapy

Single agent
novel therapies
(targeted & non-targeted)



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
~60-70%

**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
~60-70%

**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)
- 70% CR+CRh rate (16 of 23)
- 61% CR rate (14 of 23)
- 82% 12-month overall survival rate

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
~60-70%

**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

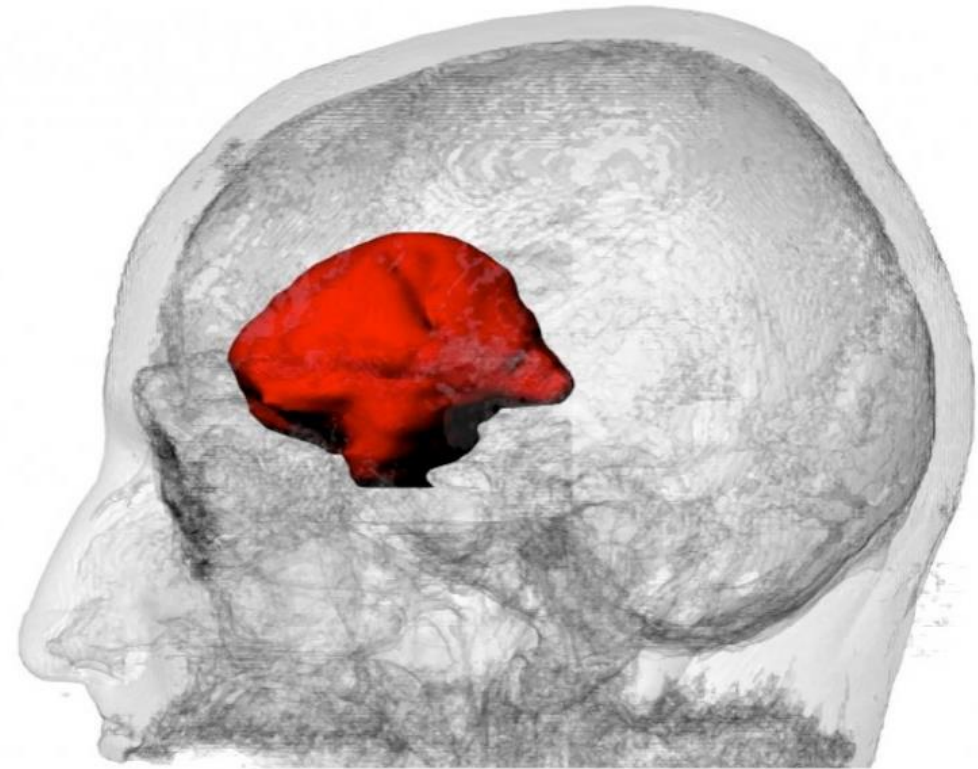
BROAD IST SUPPORT
VYXEOS™ Combination

Opportunity for an IDH1m Inhibitor in Solid Tumors

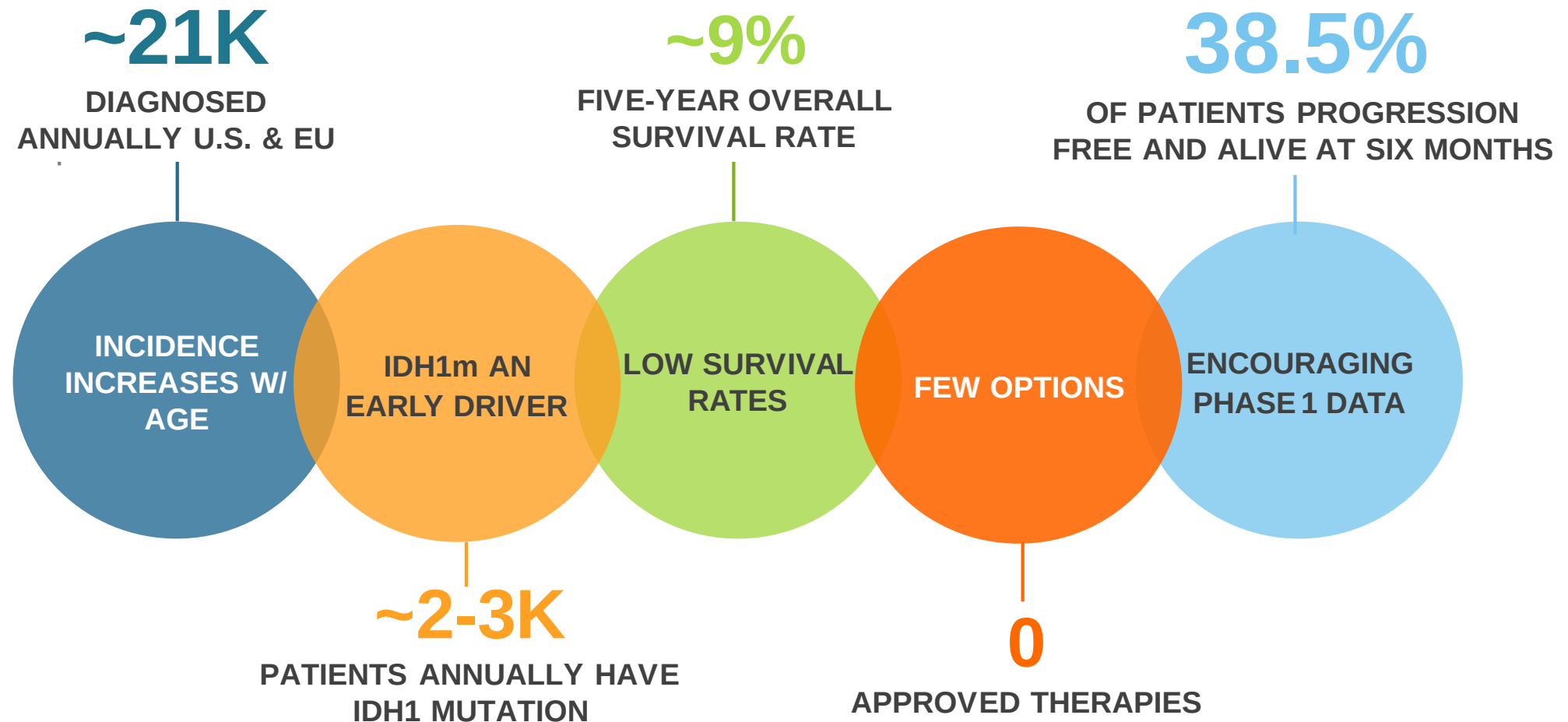
CHOLANGIOCARCINOMA



LOW GRADE GLIOMA



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

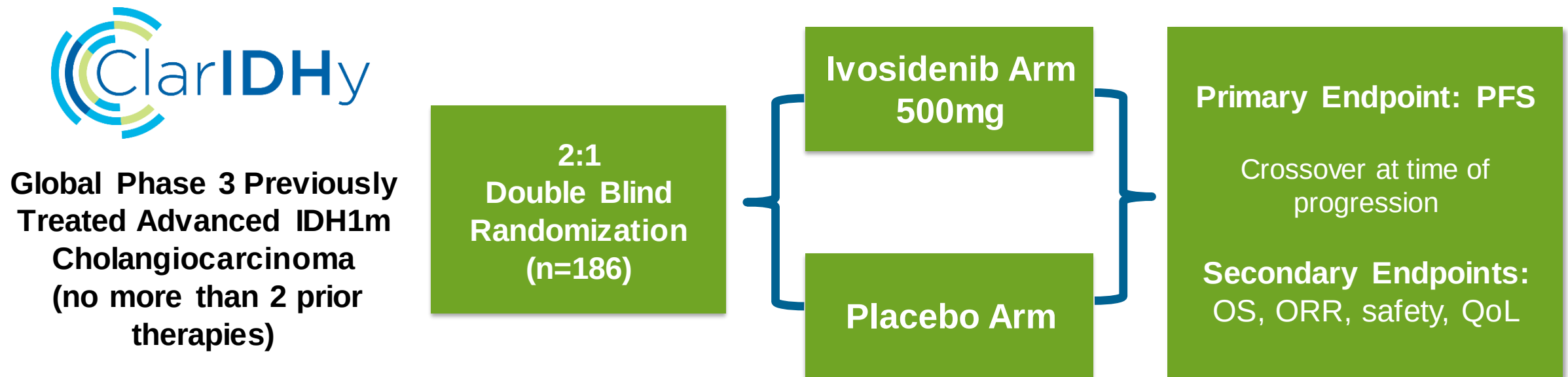


Sources: CDC National Program of Cancer Registries (NPCR); Epiphany Partners Epic Oncology; Decision Resources; Market Research; Borger DR et al. Oncologist 2012;17:72-9.; Kipp BR et al. Hum Pathol 2012;43:1552-8.; Goyal L et al. Oncologist 2015;20:1019-27; data from ASCO 2017



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

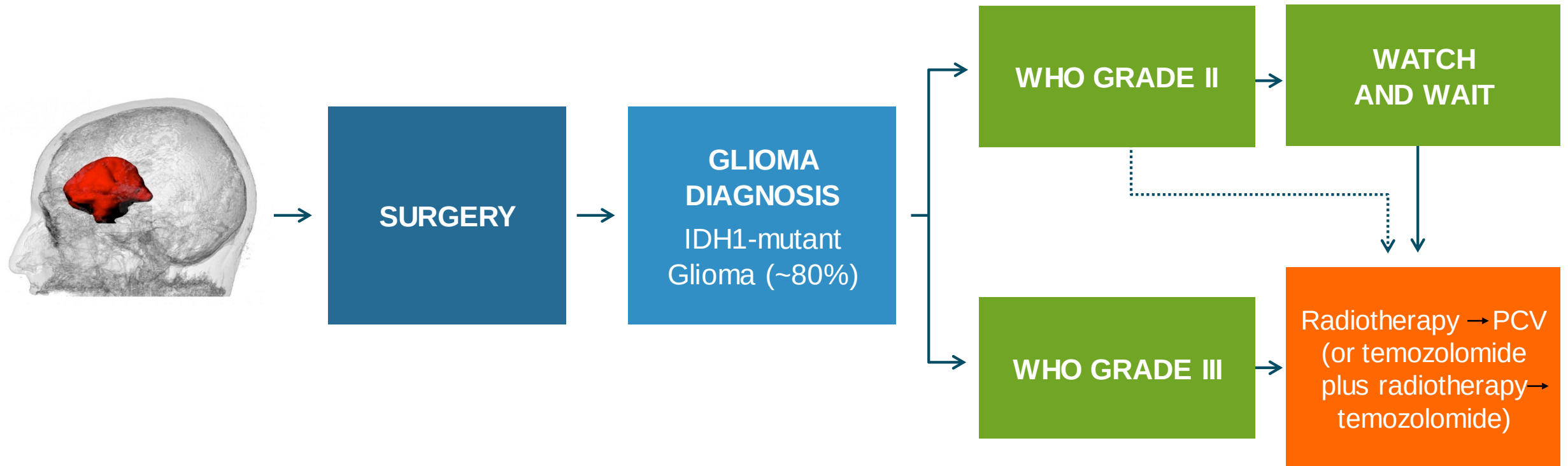


ClinicalTrials.gov Identifier: NCT02989857

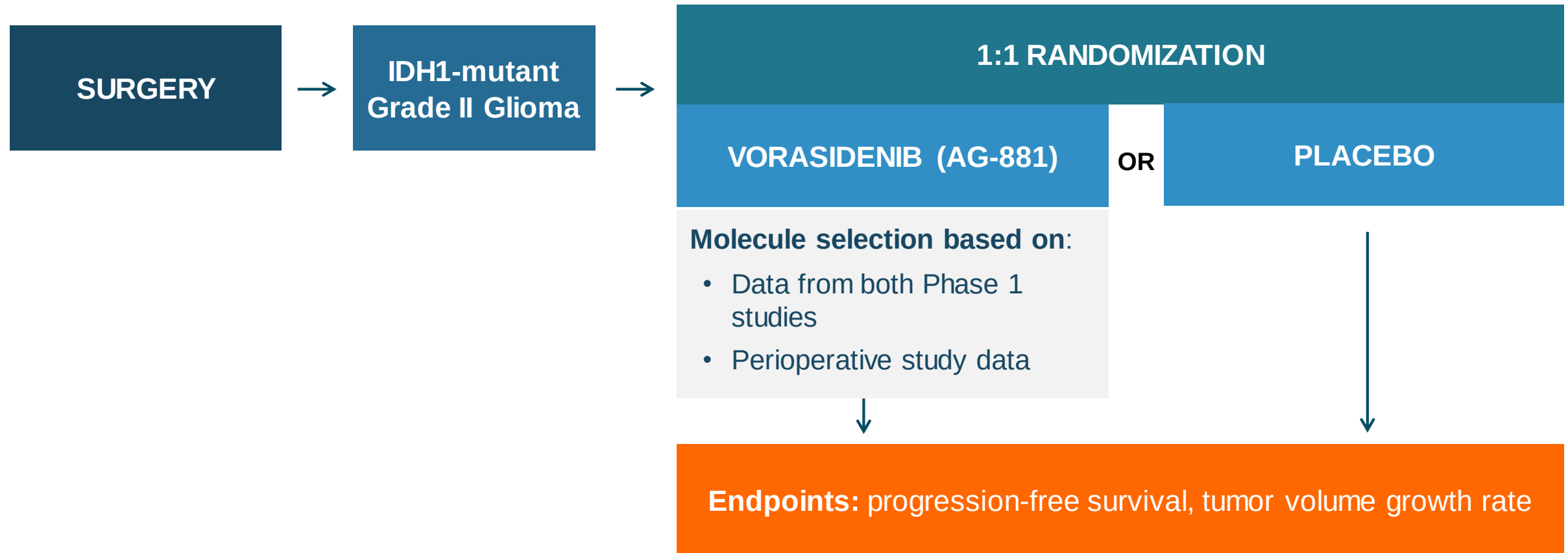
Full data from the Phase 3 ClarIDHy study of TIBSOVO® in IDH1m advanced cholangiocarcinoma submitted for presentation at ESMO



Current Treatment Paradigm for IDHm Gliomas



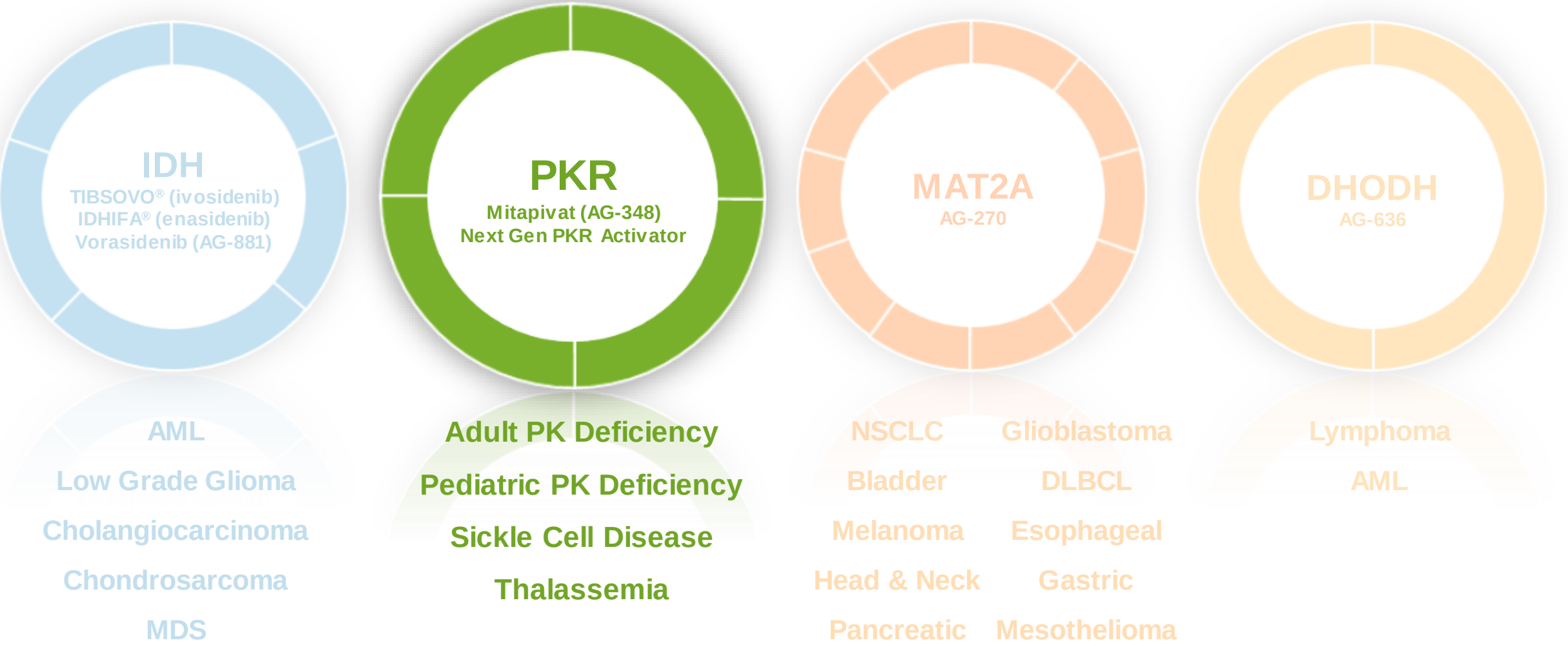
Pivotal Path in WHO Grade II Glioma: Aim to Delay Progression to Chemotherapy and/or Radiotherapy



Registration-enabling Phase 3 study of vorasidenib to initiate by year-end 2019



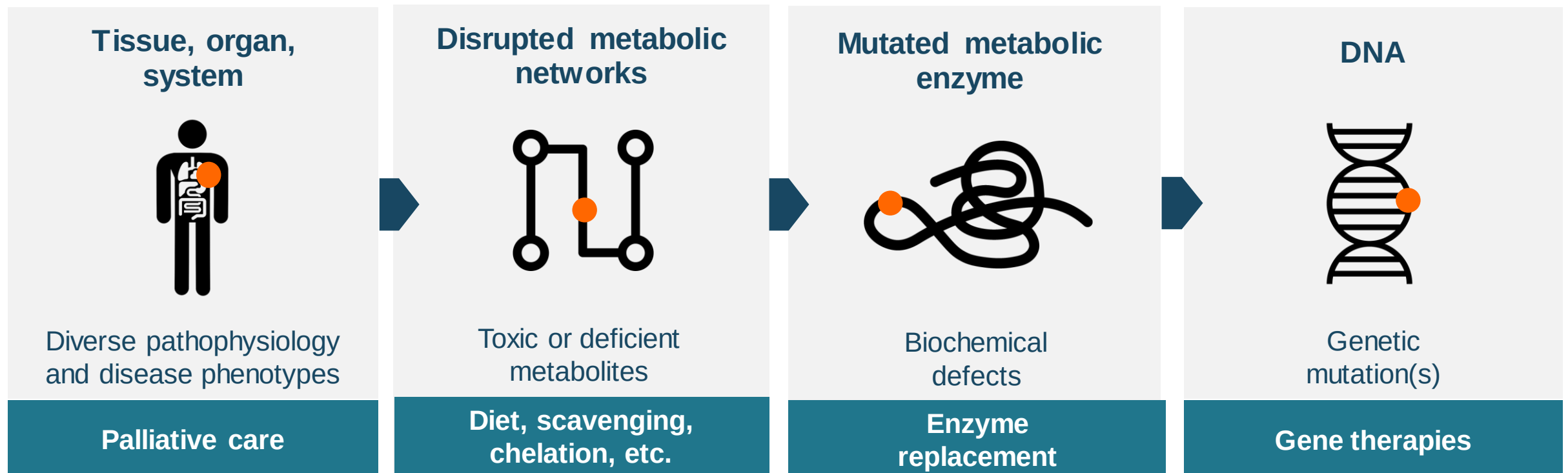
Productive Research & Discovery Engine Has Produced
Four Key Targets with Multiple Disease Opportunities



Our Approach to Rare Genetic Diseases

Part of a New Wave of Transformational Therapies

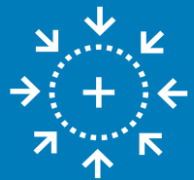
Understanding and correcting the root cause of the disease



Our Approach to Rare Genetic Diseases

Part of a New Wave of Transformational Therapies

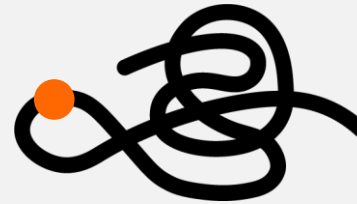
Understanding and correcting the root cause of the disease



AGIOS APPROACH

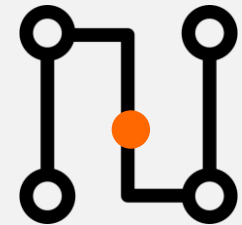
Disease-modifying small molecules targeting intracellular pathways leading to transformative outcomes for patients

Mutated metabolic enzyme



Biochemical defects

Disrupted metabolic networks



Toxic or deficient metabolites



What's Possible with PKR Activators

NOW

- Adult PK Deficiency

NEXT

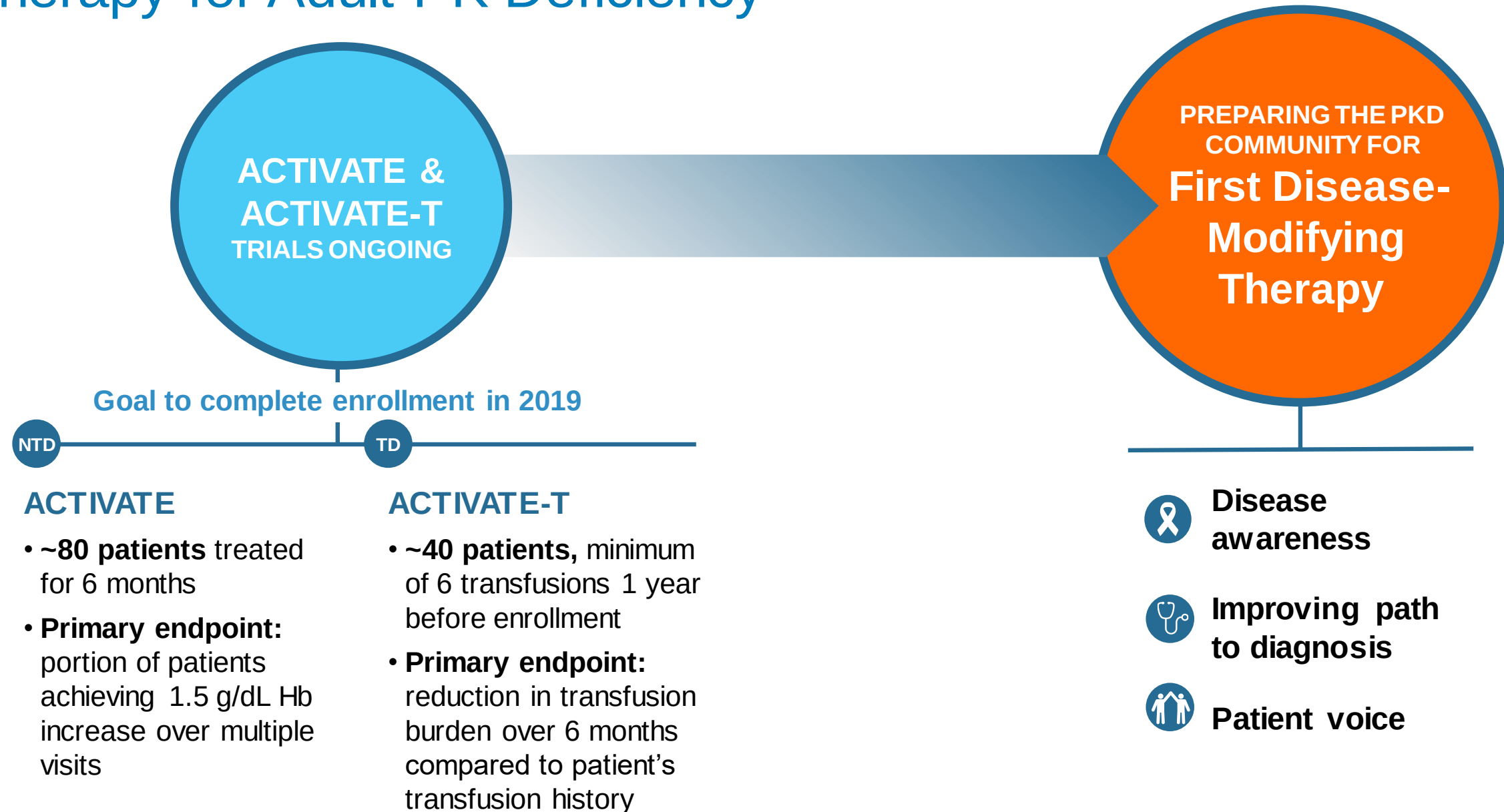
- Thalassemia
- Sickle Cell Disease

FUTURE

- Pediatric PK Deficiency



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



Broadening the Opportunity for Mitapivat in Thalassemia and Pediatric PK Deficiency 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 PK DEFICIENCY PEDIATRICS

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

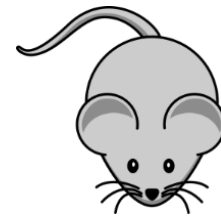


Committed to Continued Development of PKR Activators for the Treatment of Every Patient with PK Deficiency



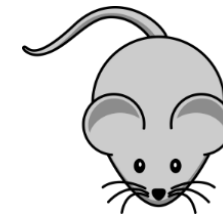
DEVELOPMENT CANDIDATE FOR A NEXT GENERATION PKR ACTIVATOR SELECTED

- 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

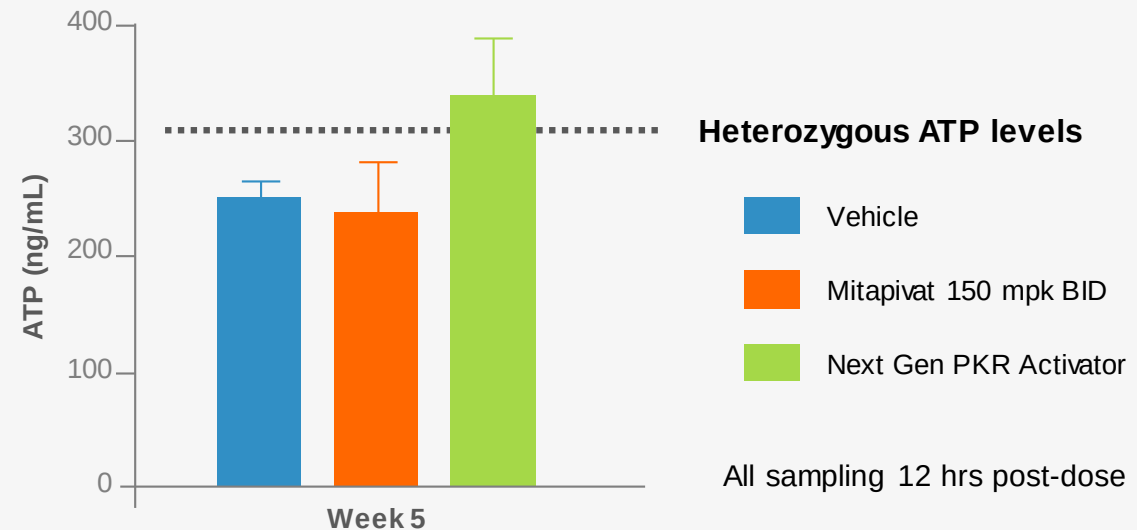


WT MOUSE

CRISPR



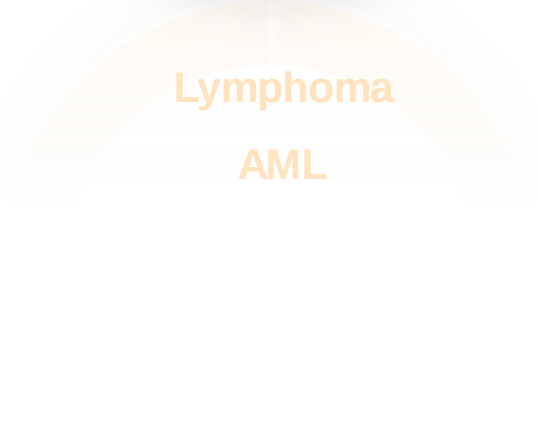
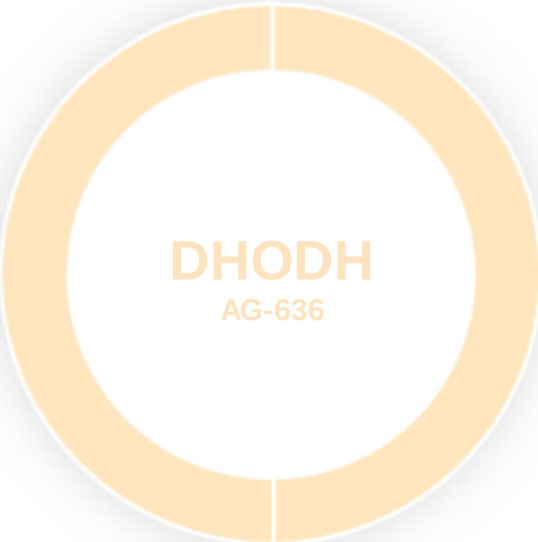
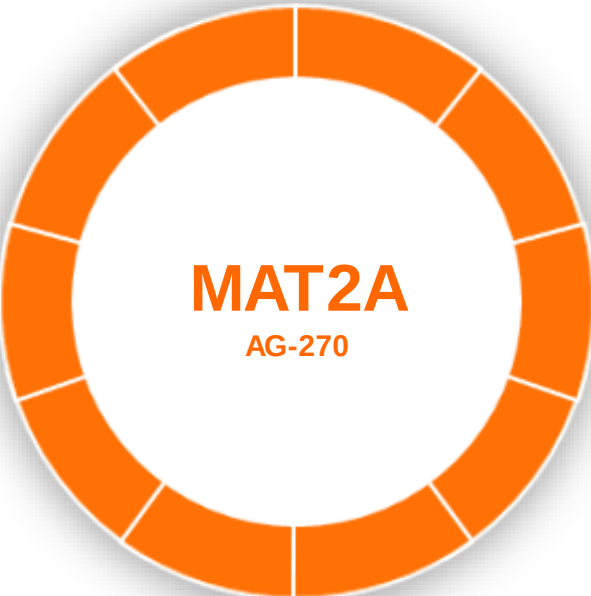
R510Q MOUSE



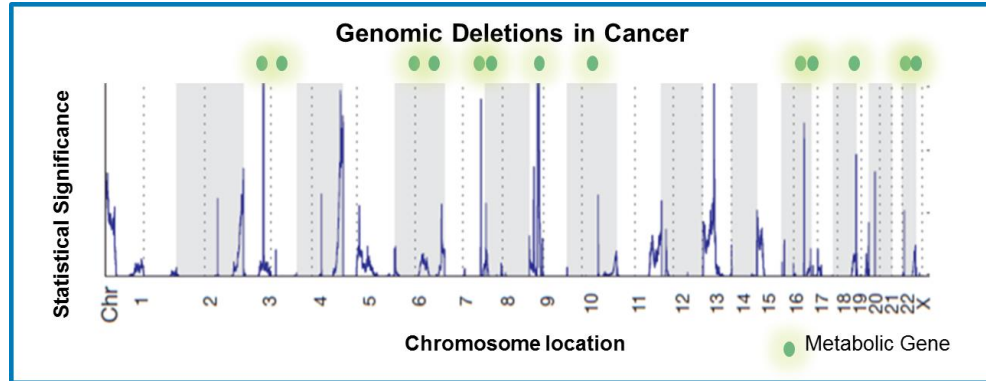
Next generation molecule superior at increasing ATP levels in a mouse model with the R510Q mutation



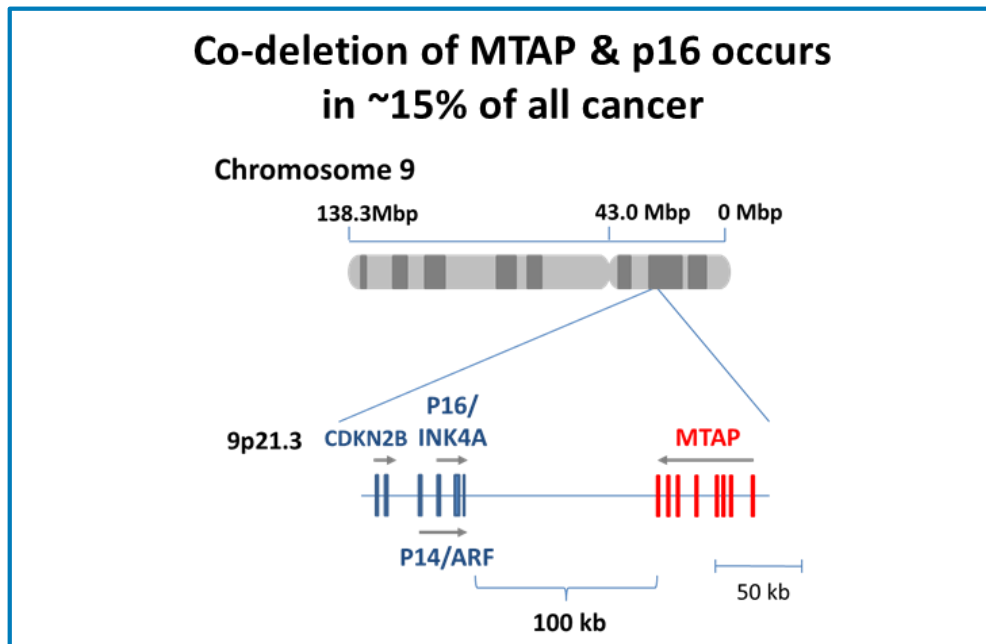
Productive Research & Discovery Engine Has Produced
Four Key Targets with Multiple Disease Opportunities



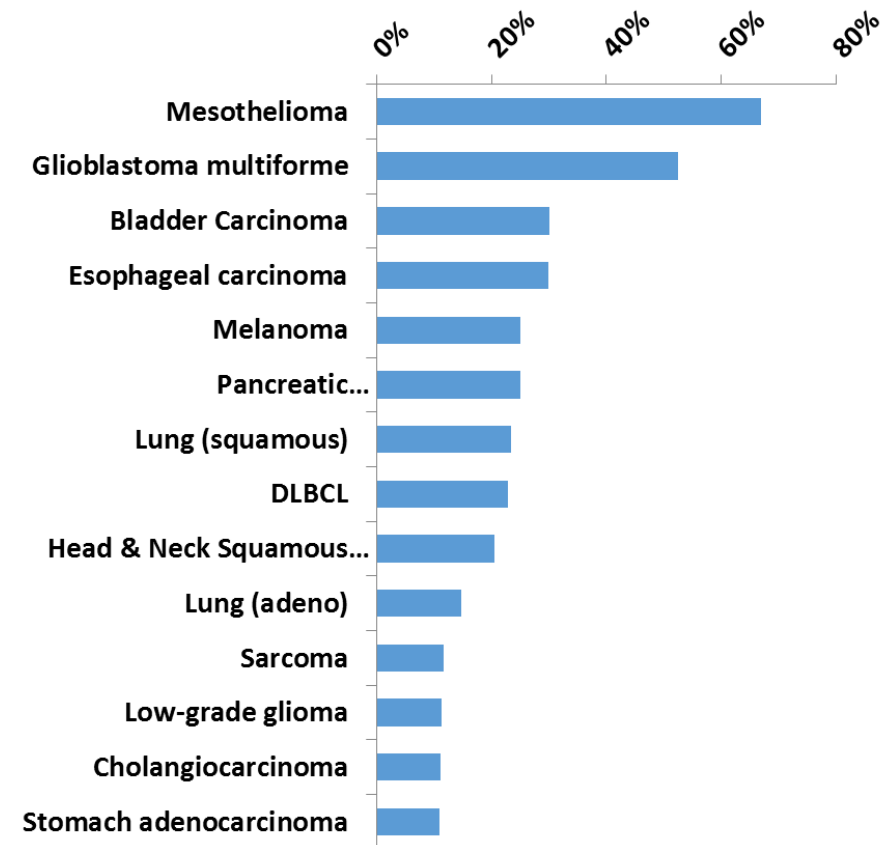
MTAP Deletions Occur in ~15% of All Cancers



Source: Adapted from Beroukhi et al Nature 2010

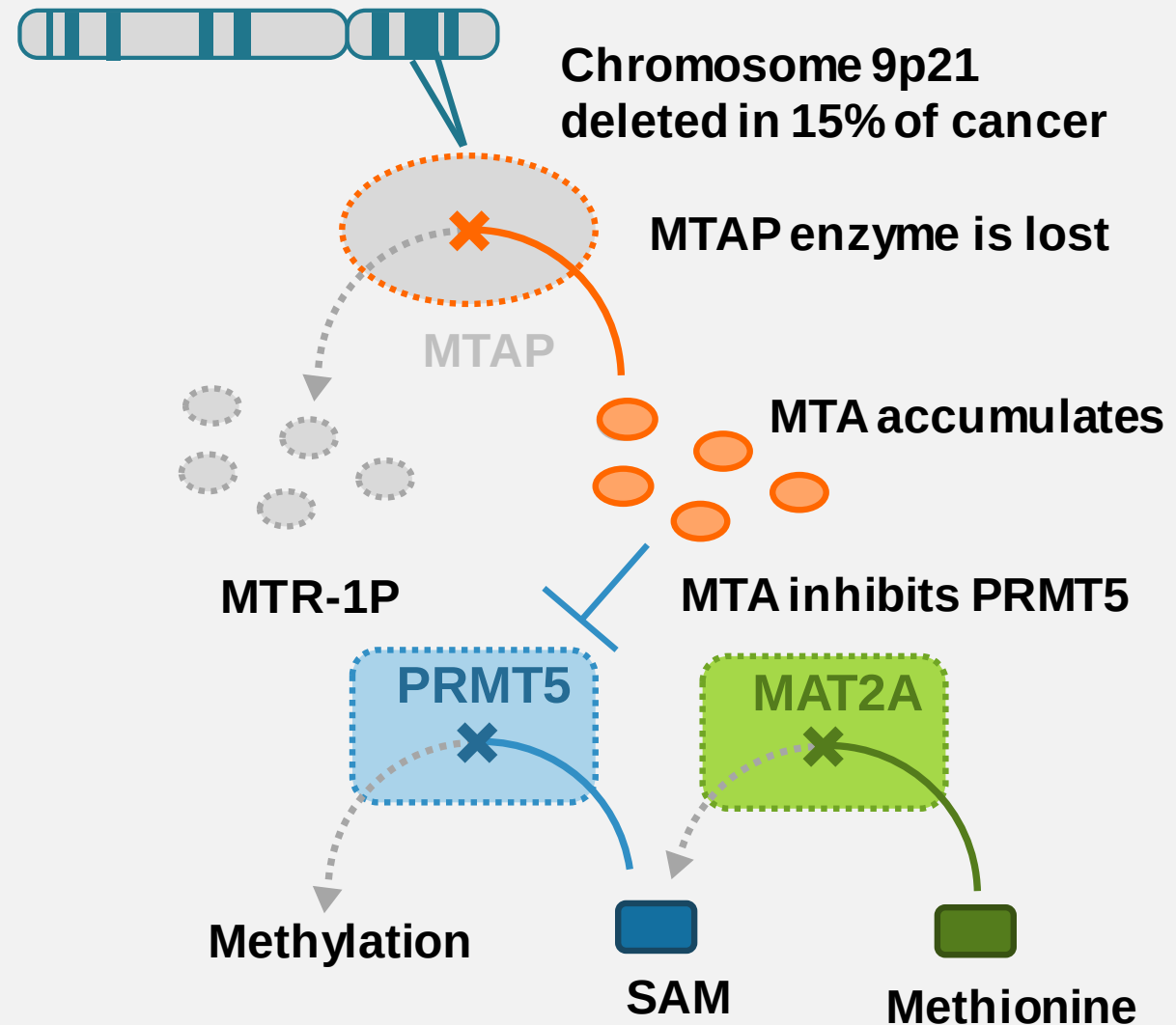


MTAP Deletion Frequency

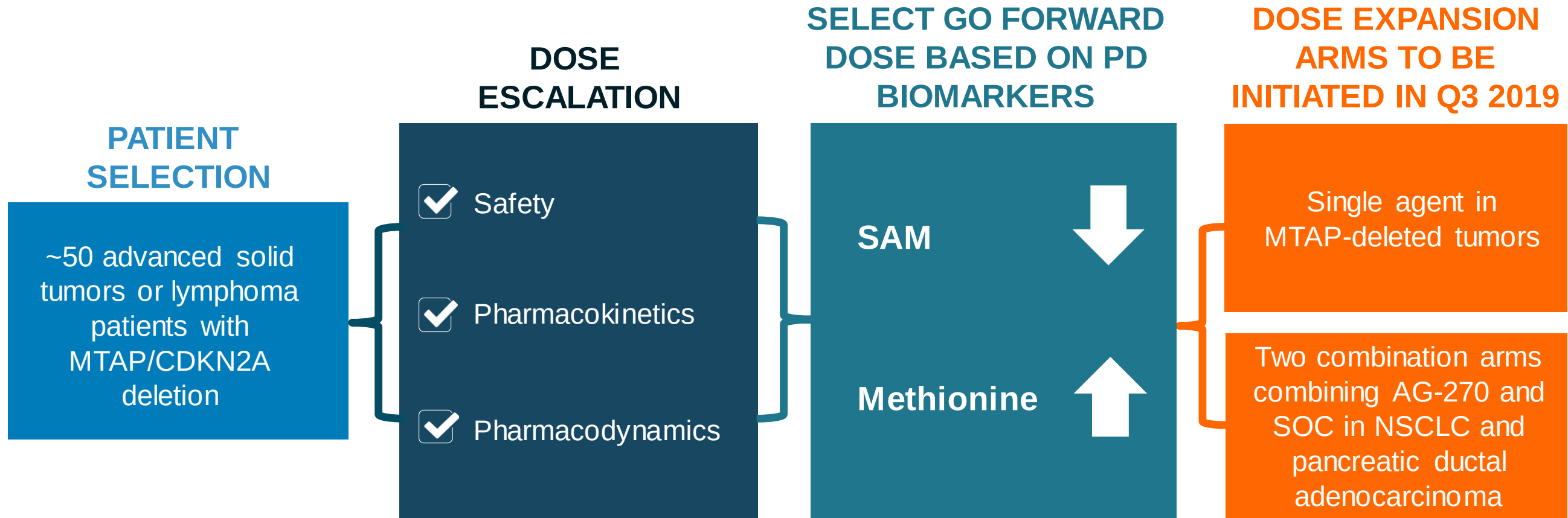


A Key Insight: Deletion of MTAP Makes Cancers Vulnerable to Targeting of MAT2A

- 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



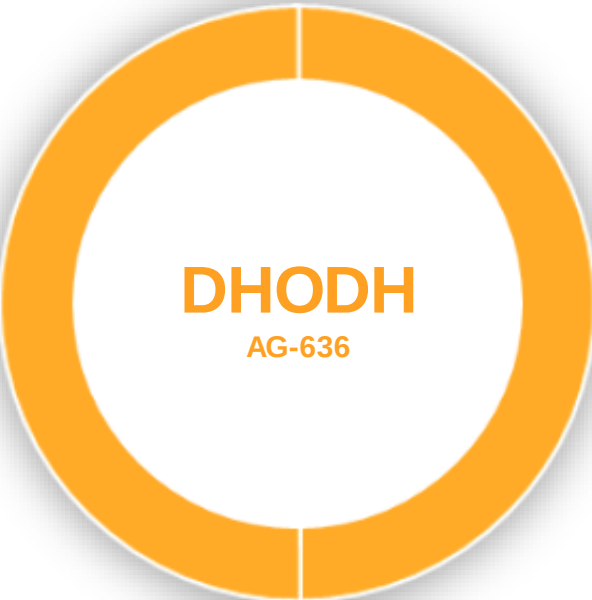
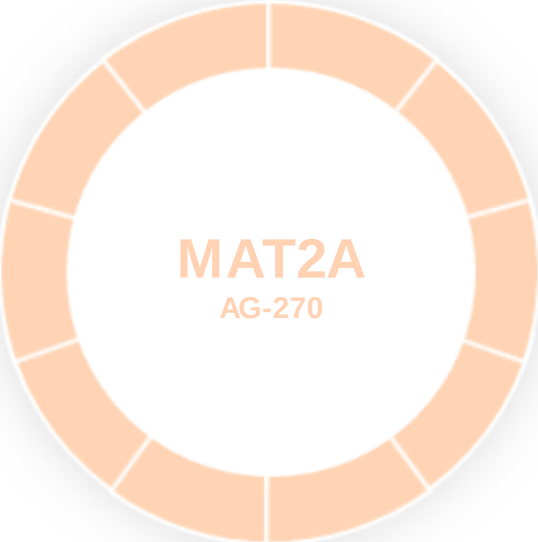
Advancing AG-270 to Next Phase of Clinical Development



ClinicalTrials.gov Identifier: NCT03435250



Productive Research & Discovery Engine Has Produced
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

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



CORPORATE



First Quarter 2019 Financial Results

Statement of Operations	Three Months Ended 3/31/19	Three Months Ended 3/31/18
Total Revenue	\$30.2M	\$8.8M
Collaboration Revenue	18.9M	7.3M
TIBSOVO® Net Sales	9.1M	--
Royalty Revenue	2.2M	1.4M
Cost of Sales	0.3M	--
Research & Development Expense	95.6M	78.2M
Selling, General & Administrative Expense	31.8M	24.6M

Balance Sheet	3/31/19	12/31/18
Cash, Cash Equivalents and Marketable Securities	\$707.8M	\$805.4M

March 31, 2019 cash balance provides runway through at least the end of 2020



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
 - Complete AG-270 Phase 1 dose-escalation and initiate expansion arms in Q3 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 Upcoming Data Presentations

- Full data from Phase 3 ClarIDHy trial of TIBSOVO® in IDH1m advanced cholangiocarcinoma submitted for presentation at ESMO
- Data from dose-escalation portion of Phase 1 trial of AG-270 in MTAP-deleted tumors in 2H 2019

