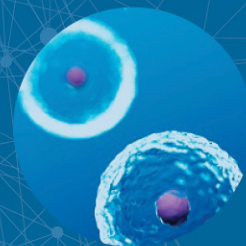
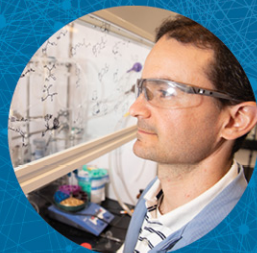




# AGIOS 2025 VISION

March 2020 Corporate Presentation





# 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), mitapivat, vorasidenib, AG-270 and AG-636; the potential benefits of Agios' product candidates; Agios's strategic vision and goals for 2025; its key milestones for 2020; its estimates regarding its balance of cash, cash equivalents and marketable securities for the year ended December 31, 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," "vision," 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; 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.



We are  
driven by our  
sense of  
urgency to  
help patients.



“On a bad day, it’s like watching some electronic toy slowly lose the battery.”  
—Tamara S., Minnesota



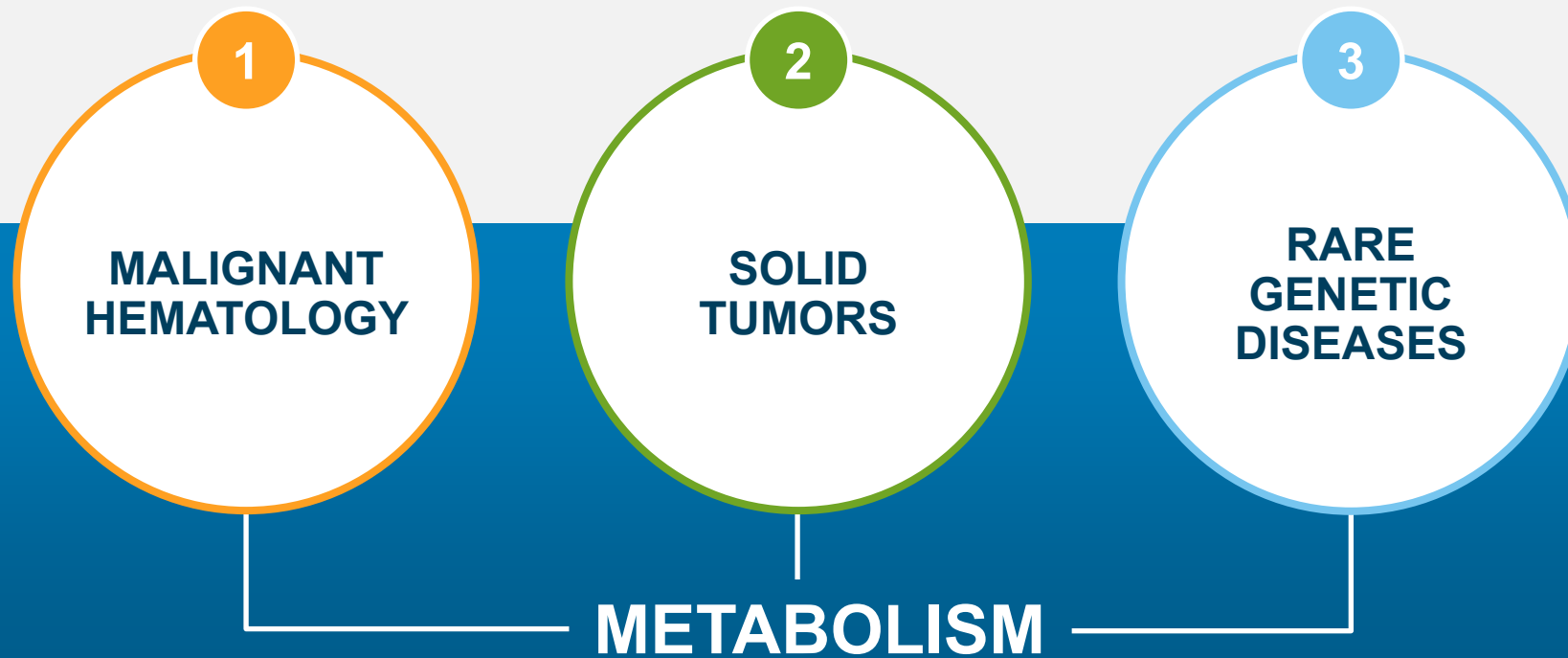
“The disease has affected my career. I spent 11 years to get a PhD in nutrition...My heart wants more but my body can’t handle it.”

**—Tamara S., Minnesota**

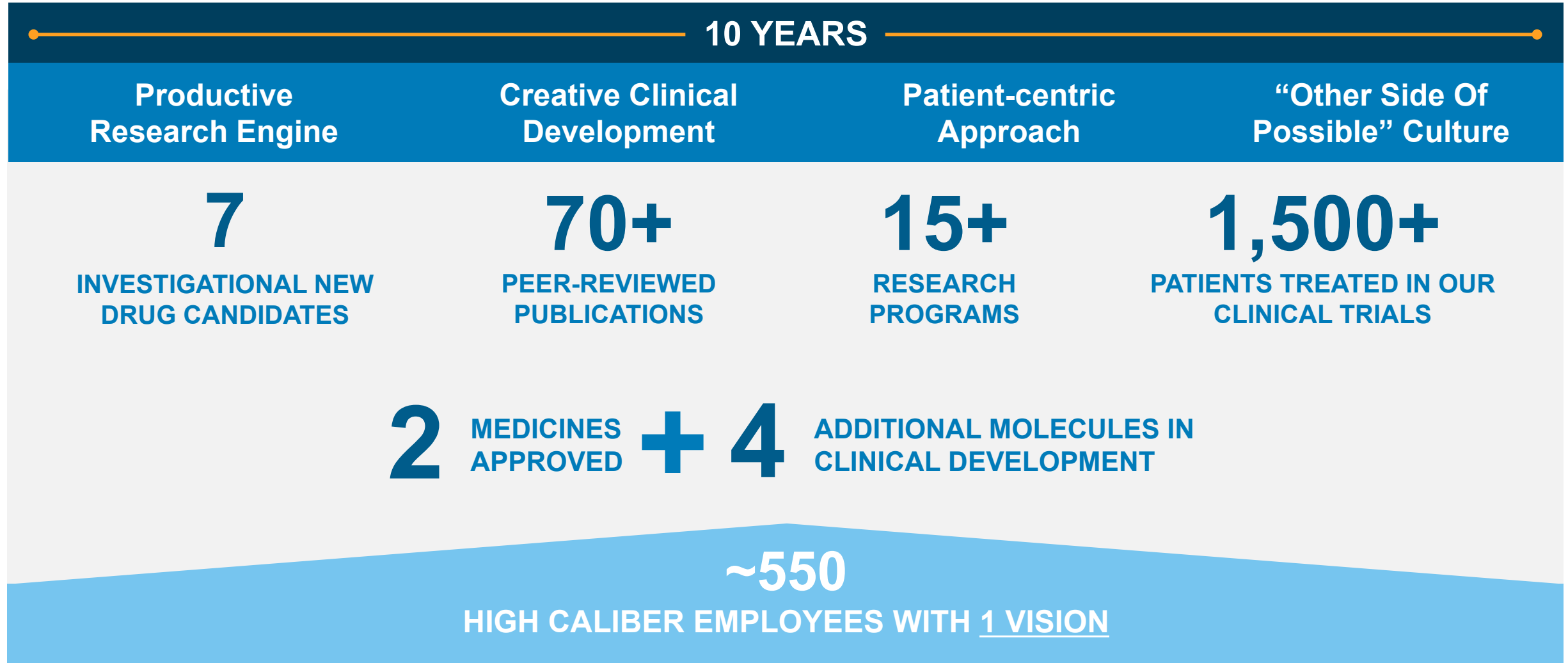
Currently 50 years old. Diagnosed with PK deficiency at the age of 6.

# Our Strategy is Clear

For more than a decade, our mission has been to create **differentiated, small molecule medicines for patients** in three focus areas – malignant hematology, solid tumors and rare genetic diseases – based on our unique expertise in **cellular metabolism** and adjacent areas of biology



# Our People and Culture Fuel Incredible Productivity, Strategic Focus and Continuity from Early Research to Market

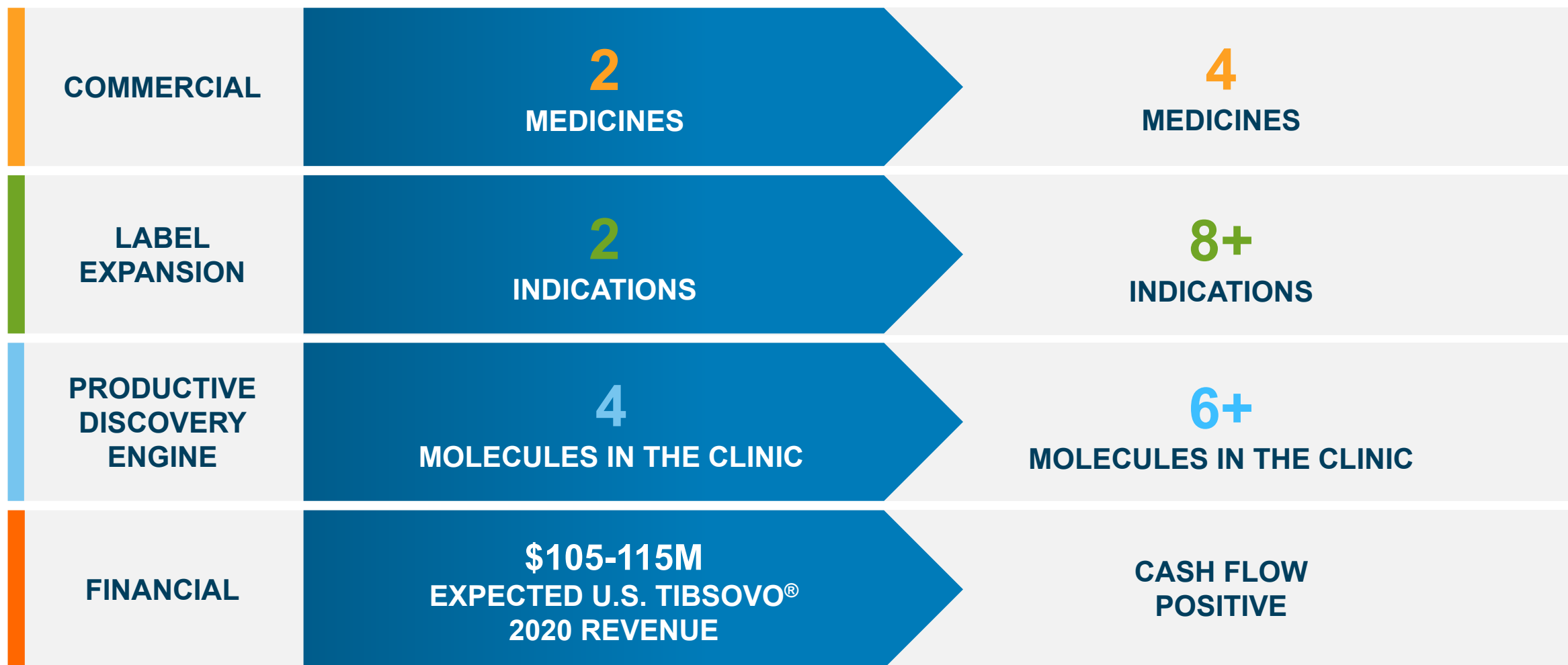




# Agios 2025 Vision: Focused Innovation. Ambitious Development. Transformative Treatments for Patients Across Three Focus Areas.

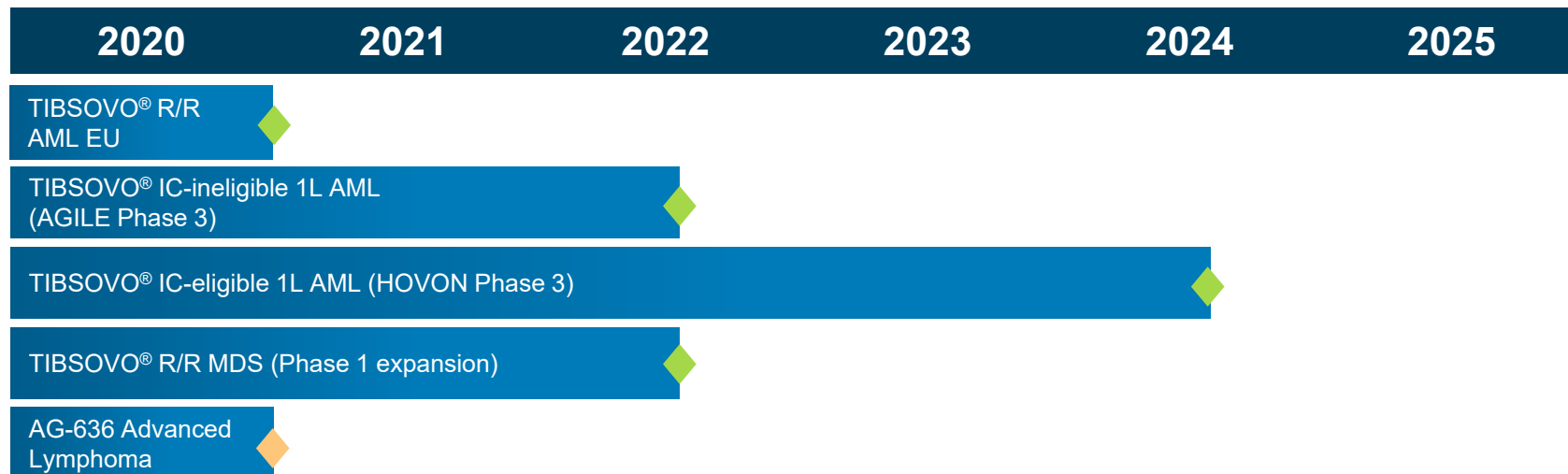
**NOW**

**2025**



# Multiple Potential Near- and Long-term Value Drivers Across All Focus Areas

## HEMATOLOGIC MALIGNANCIES



## SOLID TUMORS



## RARE GENETIC DISEASES



 Approval
  Make go/no-go decision



# Highly Productive Research Engine with Optionality Across Focus Areas

Program	Target Discovery	Target Validation	Drug Discovery	Drug Candidate
<b>Malignant Hematology</b>				
MAT2A Follow-Ons			●	
Macrophage I-O Target			●	
Tumor I-O Target			●	
Genetically Defined Heme Target			●	
Metabolic I-O Exploratory Programs	●	●		
Other Exploratory Programs	●	●		
<b>Solid Tumor</b>				
MAT2A Follow-Ons			●	
Macrophage I-O Target			●	
Tumor I-O Target			●	
Genetically Defined Solid Tumor Target			●	
Metabolic I-O Exploratory Programs	●	●		
Other Exploratory Programs	●	●		
<b>Rare Genetic Diseases</b>				
AG-946 (Pyruvate Kinase Activator Follow-On)				●
Phenylketonuria (PKU)			●	
Erythroid Porphyrria			●	
Friedreich's Ataxia			●	
Other Exploratory Programs	●	●		



Metabolic Target



Non-Metabolic Target



Metabolic and Non-Metabolic Targets



Bristol-Myers Squibb Collaboration







**CREATING MEDICINES IN  
THREE FOCUS AREAS**

1

**Malignant Hematology**

2

**Solid Tumors**

3

**Rare Genetic Diseases**





CREATING MEDICINES IN  
THREE FOCUS AREAS

1

**Malignant Hematology**

2

**Solid Tumors**

3

**Rare Genetic Diseases**

# Significant Growth Potential in Malignant Hematology

**~4K**

**PATIENTS IN  
U.S. & EU**

**IDH1 Mutant Acute Myeloid  
Leukemia (AML)**

**TIBSOVO®**

<b>R/R AML</b>	U.S. Approval; MAA Under Review
<b>1L Monotherapy</b>	U.S. Approval
<b>1L HMA Combo</b>	Phase 3
<b>1L 7+3 Combo</b>	Phase 3

**<1K**

**PATIENTS IN  
U.S.**

**IDH1 Mutant Myelodysplastic  
Syndrome (MDS)**

**TIBSOVO®**

<b>R/R MDS</b>	Phase 1 Expansion
----------------	-------------------

**~55K**

**PATIENTS IN  
U.S. & EU**

**Mantle Cell and Diffuse Large  
B Cell Lymphoma**

**AG-636**

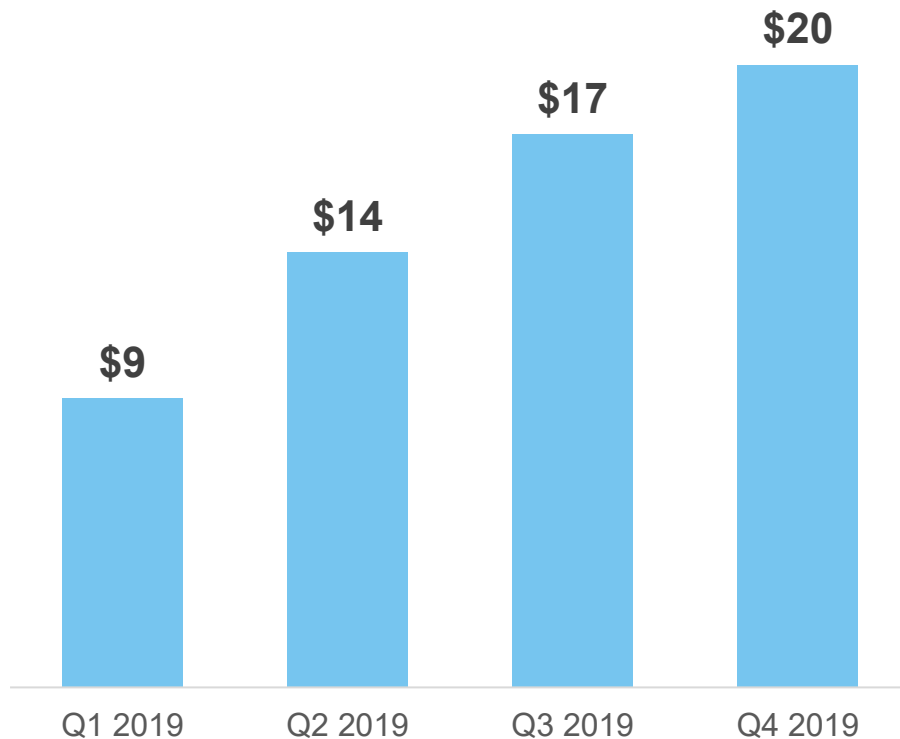
<b>R/R Lymphoma</b>	Phase 1
---------------------	---------





# Successful TIBSOVO® Launch in R/R and Frontline AML Result of Focused Commercial Effort

**TIBSOVO® Revenue**  
(in millions)



**\$60M**

Full Year 2019 Product Revenue



**\$105 – 115M**

U.S. Net Sales Guidance for 2020



**~515**

Unique Prescribers as of Q4 2019



**>1,000**

Patients Treated Since Launch

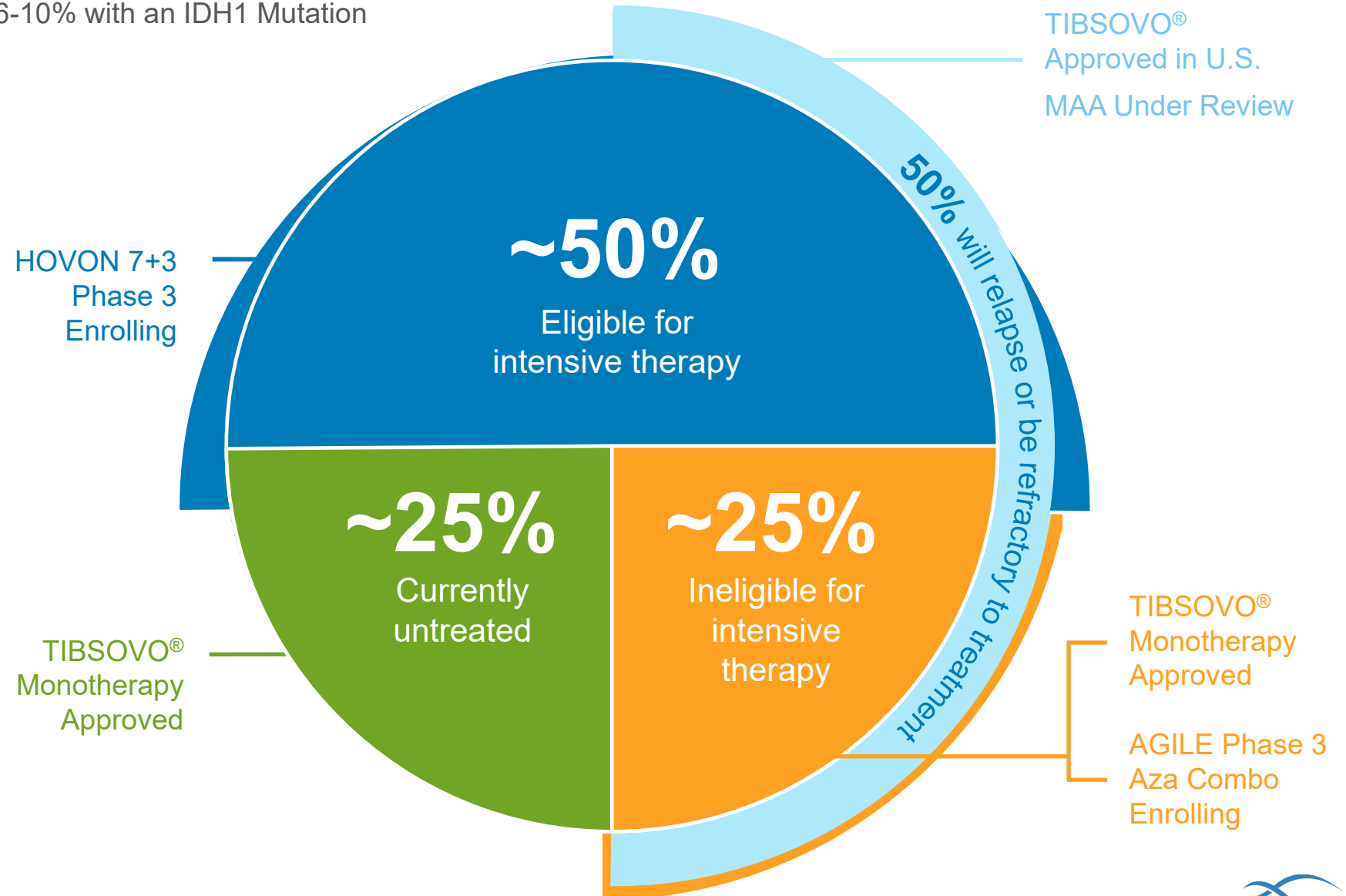
Source: Agios estimates



# 50K AML Patients Diagnosed Per Year in U.S. and EU

6-10% with an IDH1 Mutation

Advancing  
Toward Largest  
Opportunity for  
mIDH1 AML:  
Intensive and  
Non-Intensive  
Therapy  
Combinations



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







CREATING MEDICINES IN  
THREE FOCUS AREAS

1

**Malignant Hematology**

2

**Solid Tumors**

3

**Rare Genetic Diseases**



# Four Distinct Solid Tumor Opportunities Across Three Clinical Molecules

**~2-3K**

**PATIENTS IN  
U.S. & EU**

**IDH1 Mutant  
Cholangiocarcinoma**

**TIBSOVO®**

**R/R Cholangio**

**sNDA 2020**

**~9K**

**PATIENTS IN  
U.S. & EU**

**IDH Mutant  
Low Grade Glioma**

**Vorasidenib**

**Low-grade Glioma**

**Phase 3**

**~9K**

**PATIENTS  
IN U.S.**

**MTAP-Deleted Non-  
Small Cell Lung Cancer**

**AG-270**

**2nd Line NSCLC**

**Phase 1  
Combo**

**~10K**

**PATIENTS  
IN U.S.**

**MTAP-Deleted  
Pancreatic Cancer**

**AG-270**

**1st or 2nd Line  
Pancreatic Cancer**

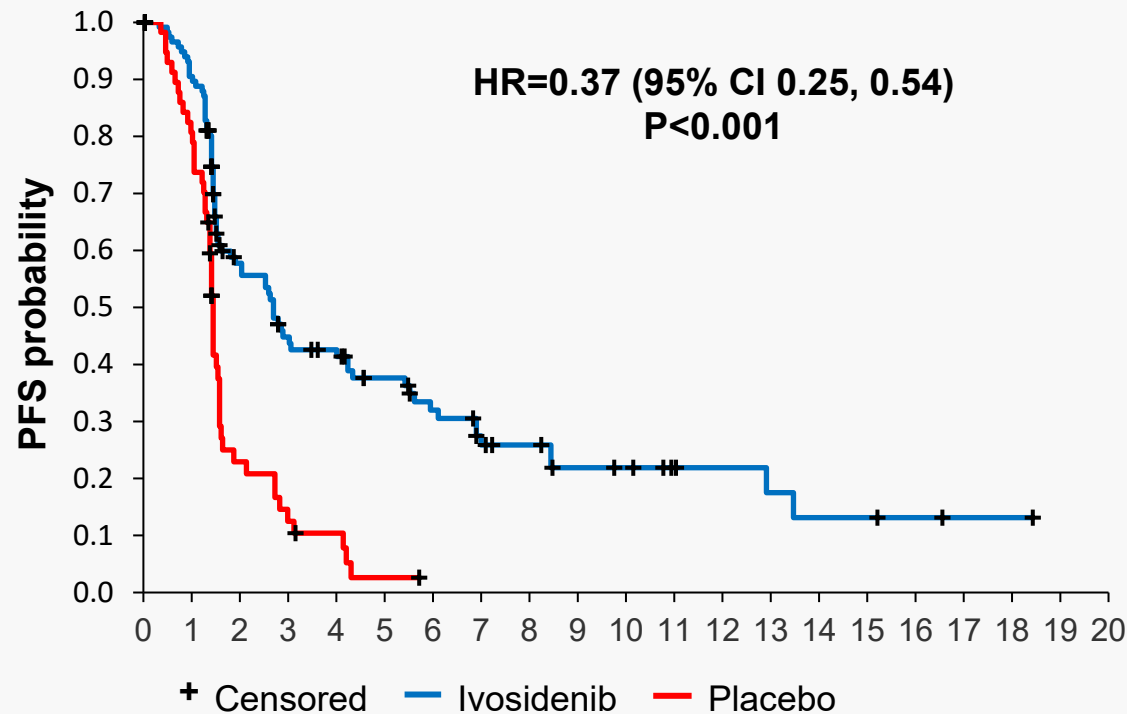
**Phase 1  
Combo**



# Established Utility of IDH Inhibition in Solid Tumors with Positive ClarIDHy Phase 3 Study of TIBSOVO® in Second-line or Later Cholangiocarcinoma

Mature OS from ClarIDHy Phase 3 expected mid-2020; sNDA planned by YE

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



LOW  
SURVIVAL  
RATES

~9%  
FIVE-YEAR  
OVERALL  
SURVIVAL  
RATE

FEW  
TREATMENT  
OPTIONS

0  
APPROVED  
THERAPIES  
FOR mIDH1  
PATIENTS

POSITIVE  
CLARIDHY  
RESULTS

63%  
REDUCTION IN  
RISK OF DISEASE  
PROGRESSION OR  
DEATH FOR  
PATIENTS  
TREATED W/  
TIBSOVO®



# Global Phase 3 INDIGO Study of Vorasidenib in IDH Mutant Low-Grade Glioma Open and Enrolling

**SIGNIFICANT  
2-HG  
SUPPRESSION**

**>90%**  
2-HG  
SUPPRESSION IN  
RESECTED  
mIDH1 GLIOMAS  
ACROSS ALL  
DOSES TESTED

**IMPRESSIVE  
PRELIMINARY  
EFFICACY  
DATA**

**33% ORR**  
IN THE  
VORASIDENIB  
ARM OF THE  
PERIOPERATIVE  
STUDY

**ENCOURAGING  
PHASE 1 DATA**

**22 mo.**  
MEDIAN  
TREATMENT  
DURATION IN  
VORASIDENIB  
PHASE 1



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

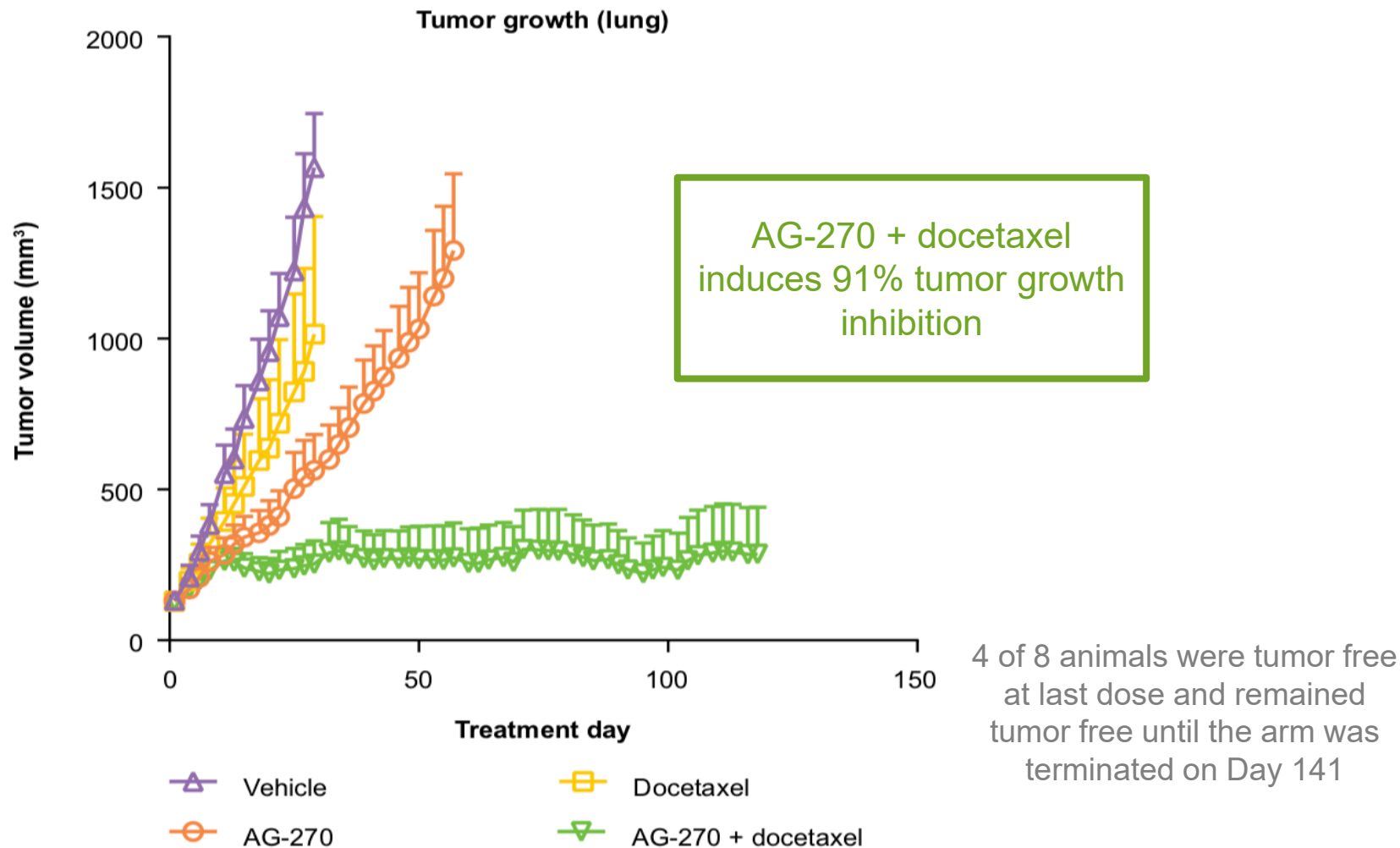
**Primary:** Progression free survival (by BIRC)

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





# AG-270, MAT2A Inhibitor, Preclinical Data Supports Combination with Taxanes; Two Phase 1 Combination Arms Enrolling Patients



Source: Data presented at AACR-NCI-EORTC 2019

## PHASE 1 COMBINATION ARMS INITIATED

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

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





CREATING MEDICINES IN THREE  
FOCUS AREAS

1

**Malignant Hematology**

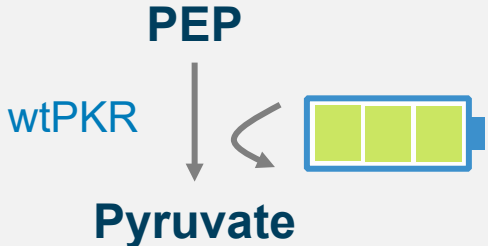

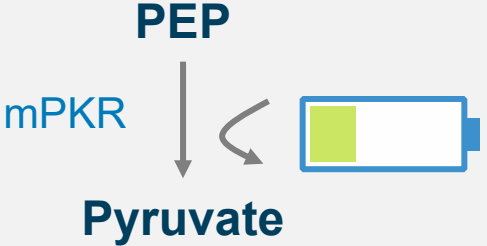

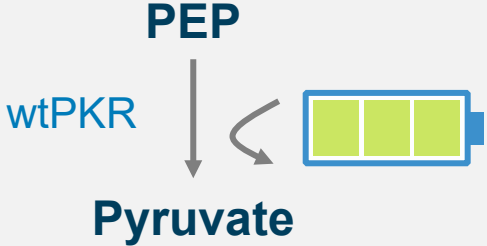
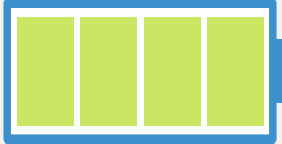
2

**Solid Tumors**

3

**Rare Genetic Diseases**

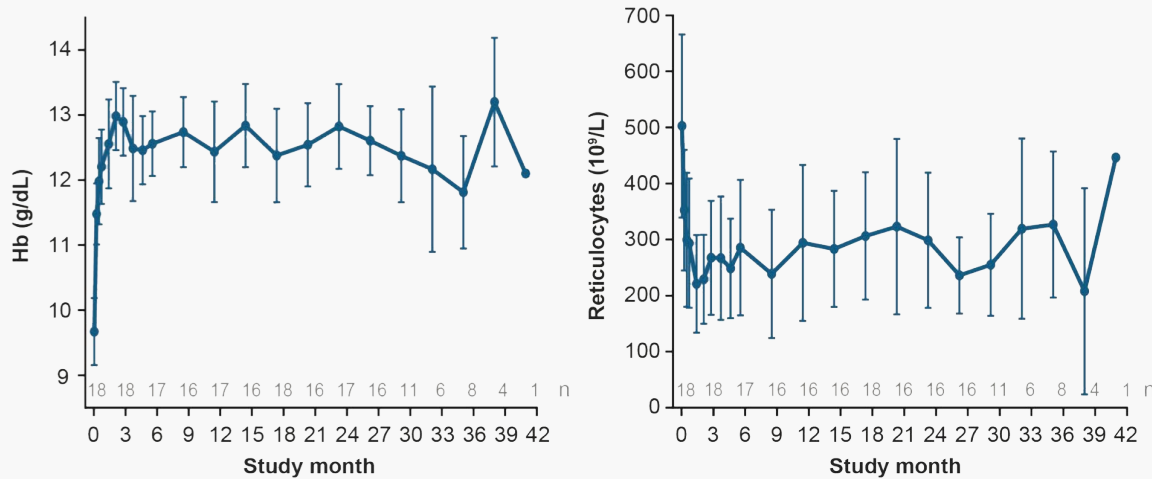
# PKR Activation Represents Unique Mechanism of Action with Potential to Address Broad Range of Hemolytic Anemias

Normal Red Cell	Pyruvate Kinase Deficiency	Other Hemolytic Anemias
 <p>PEP</p> <p>wtPKR</p> <p>Pyruvate</p> <p>Cellular demand: </p>	 <p>PEP</p> <p>mPKR</p> <p>Pyruvate</p> <p>Cellular demand: </p>	 <p>PEP</p> <p>wtPKR</p> <p>Pyruvate</p> <p>Cellular demand: </p>
<b>ATP production meets demand</b>	<b>Inadequate production: ATP deficiency</b>	<b>Increased demand: ATP deficiency</b>
	<ul style="list-style-type: none"><li>▪ Proof-of-concept achieved</li><li>▪ Adult PK deficiency approval expected in 2021</li><li>▪ Pediatric PK deficiency pivotal strategy to be finalized in 2020</li></ul>	<ul style="list-style-type: none"><li>▪ Thalassemia proof-of-concept achieved</li><li>▪ NIH sponsored trial in sickle cell disease ongoing</li></ul>



# Mitapivat has Potential to be First Disease-modifying Therapy for Patients with PK Deficiency

## Improvements in Hemoglobin and Other Hemolysis Markers Maintained for More Than 3 Years in Responding Patients from DRIVE PK Extension



Chronic daily dosing with mitapivat for a median of 3 years and up to 42 months was well tolerated

COMPLICATIONS & COMORBIDITIES REGARDLESS OF TRANSFUSION STATUS

HIGHER LIFETIME RATES OF PULMONARY HYPERTENSION, OSTEOPOROSIS, AND LIVER CIRRHOSIS

SUPPORTIVE CARE ONLY

0 APPROVED THERAPIES

HIGH RISK OF IRON OVERLOAD

38% OF PATIENTS NOT RECEIVING REGULAR TRANSFUSIONS EXPERIENCE IRON OVERLOAD

Source: Data presented at ASH 2019; van Beers EJ, et al. Haematologica. 2019;104(2):e51-e53.



## Clinical Proof-of-concept for Mitapivat Established in Non-transfusion-dependent Thalassemia

7 of 8 efficacy evaluable patients achieved a hemoglobin increase of  $\geq 1.0$  g/dL from baseline in at least one assessment (weeks 4 – 12)

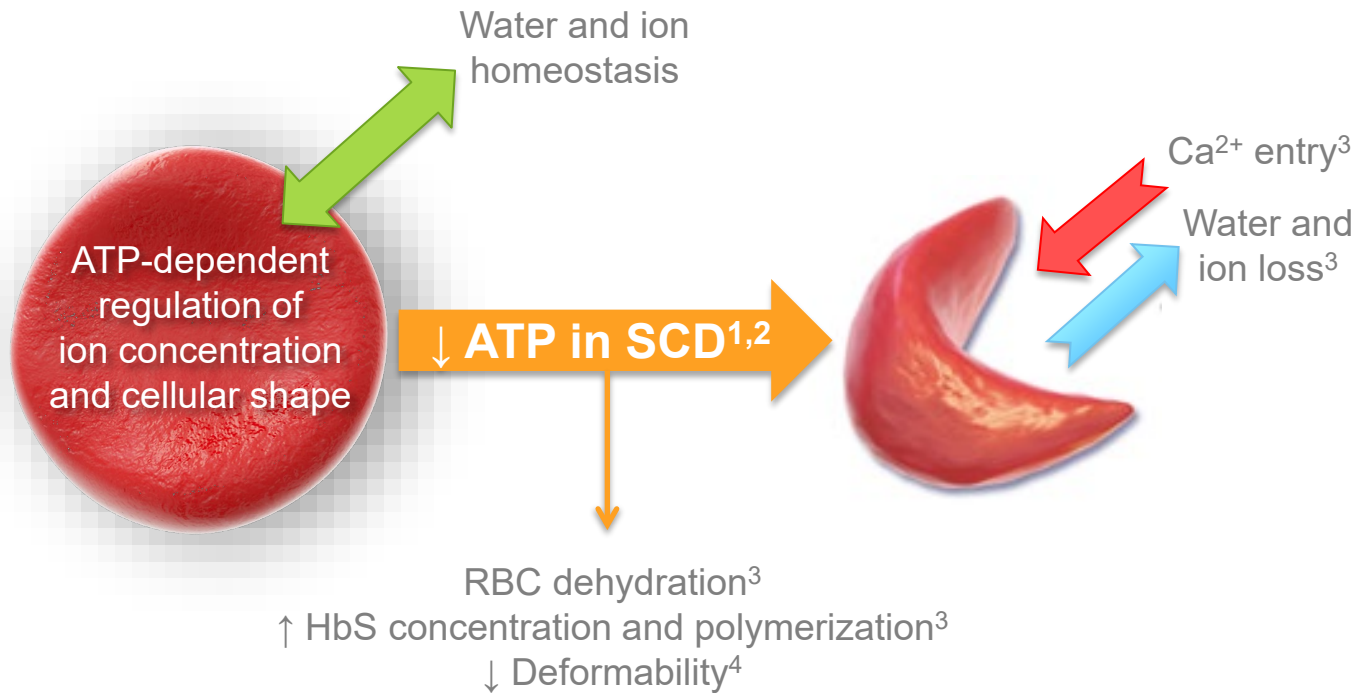
In responding patients, the mean hemoglobin increase from baseline was 1.76 g/dL (range, 0.9 – 3.3 g/dL)

Majority of adverse events were Grade 1 or 2 and consistent with previously published Phase 2 data for mitapivat in patients with PK deficiency

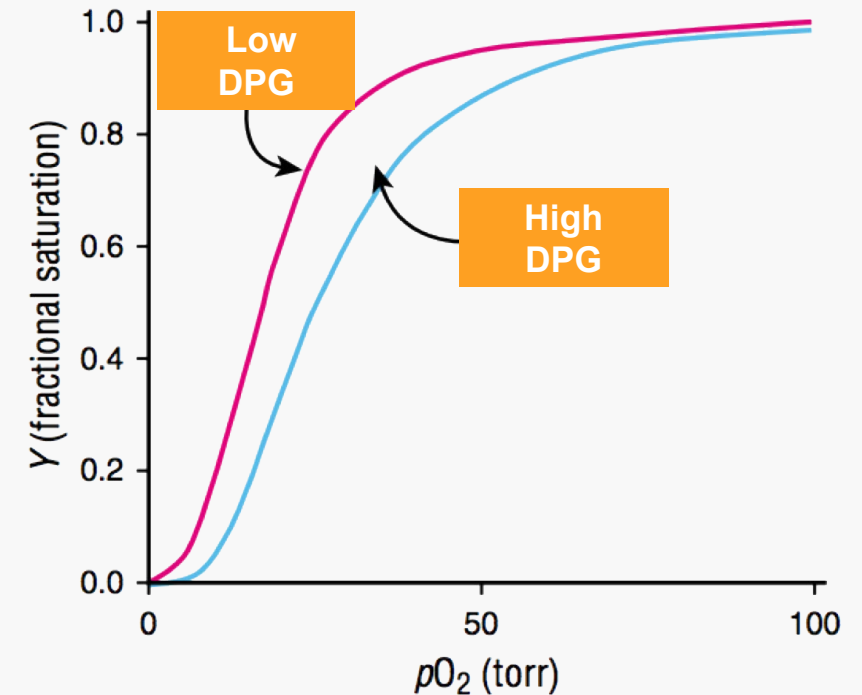
Updated Phase 2 thalassemia data to be submitted for presentation at EHA and pivotal strategy to be finalized by YE 2020



# Therapeutic Hypothesis for Wildtype PKR Activation in Sickle Cell Disease: 2,3-DPG and ATP Modulation Improves Anemia and Reduces Sickling



## 2,3-DPG Shifts the Oxygen Saturation Curve



ATP, adenosine triphosphate; HbS, sickle cell hemoglobin; RBC, red blood cell; SCD, sickle cell disease.

1. Palek J, Liu SC. J Supramol Struct. 1979;10(1):79-96. 2. Glader BE, et al. Br J Haematol. 1978;40(4):527-32.

3. Bogdanova A, et al. Int J Mol Sci. 2013;14(5):9848-72. 4. Park Y, et al. Proc Natl Acad Sci USA. 2010;107(4):1289-94.



# PKR Activation Has Potential Broad Utility Across Hemolytic Anemias

**~3-8K**  
**PATIENTS IN**  
**U.S. & EU**

**Pyruvate Kinase Deficiency**

<b>NTD Adult PKD</b>	Phase 3 Enrollment Closed
----------------------	---------------------------

<b>TD Adult PKD</b>	Phase 3 Enrollment Closed
---------------------	---------------------------

<b>Pediatric PKD</b>	Pivotal Plan by YE
----------------------	--------------------

**~18-  
23K**  
**PATIENTS IN**  
**U.S. & EU**

**$\beta$ - and  $\alpha$ -Thalassemia**

<b>NTD <math>\beta</math>- and <math>\alpha</math>-Thalassemia</b>	Phase 2
--	---------

<b>Thalassemia</b>	Pivotal Plan by YE
--------------------	--------------------

**~120-  
135K**  
**PATIENTS IN**  
**U.S. & EU**

**Sickle Cell Disease**

<b>Adult SCD</b>	NIH CRADA
------------------	-----------







**CREATING MEDICINES IN  
THREE FOCUS AREAS**

1

**Malignant Hematology**

2

**Solid Tumors**

3

**Rare Genetic Diseases**

# Agios 2020 Key Milestones

## HEMATOLOGIC MALIGNANCIES

- Achieve full-year U.S. revenue for TIBSOVO® \$105-115M
- Receive CHMP opinion for TIBSOVO® in mIDH1 relapsed/refractory AML
- Complete enrollment in AGILE Phase 3 trial of TIBSOVO® + azacitidine in frontline mIDH1 AML
- Complete enrollment in MDS arm of TIBSOVO® Phase 1

## SOLID TUMORS

- File sNDA for TIBSOVO® in mIDH1 previously treated cholangiocarcinoma

## RARE GENETIC DISEASES

- Topline data in PK deficiency from ACTIVATE and ACTIVATE-T
- Present data from mitapivat Phase 2 thalassemia study and finalize pivotal trial strategy in thalassemia
- Achieve proof-of-concept for mitapivat in sickle cell disease
- Initiate first-in-human study for next generation PKR activator, AG-946

## RESEARCH

- Achieve at least 1 new development candidate







# AGIOS 2025 VISION:

Focused Innovation. Ambitious Development.  
Transformative Treatments for Patients Across Three Focus Areas.

**4**

**MEDICINES**

**8+**

**INDICATIONS**

**6+**

**MOLECULES  
IN THE CLINIC**

**\$**

**CASH FLOW  
POSITIVE**