UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 4, 2018

Agios Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-36014**	**26-0662915**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

88 Sidney Street, Cambridge, MA	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 649-8600

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

☐ Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

☐ If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 2.02 Results of Operations and Financial Condition.

On May 4, 2018, Agios Pharmaceuticals, Inc. (the "Company") issued a press release announcing its results for the quarter ended March 31, 2018. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information responsive to Item 2.02 of this Form 8-K, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure.

On May 4, 2018, the Company intends to make a slide presentation at its Investor Day. The slide presentation is being furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information responsive to Item 7.01 of this Form 8-K, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press release issued May 4, 2018.
99.2	Form of Presentation dated May 4, 2018

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

AGIOS PHARMACEUTICALS, INC.

Date: May 4, 2018

By: /s/ David P. Schenkein
David P. Schenkein, M.D.
President and Chief Executive Officer

Exhibit 99.1

Agios Provides Business Update on Discovery Research Strategy and Pipeline, Progress on Clinical Programs, Commercial Launch Preparations and Reports First Quarter 2018 Financial Results at Investor Day

– Commercial Infrastructure In Place Ahead of August 21, 2018 PDUFA Action Date for TIBSOVO® (Ivosidenib) for IDH1m R/R AML –

– Clinical Portfolio Advancing with Four Compounds in Development and Five Pivotal Trials Ongoing or Planned Across Three Distinct Disease Areas –

– Drug Discovery Platform Poised to Deliver New Research Programs with Next IND Expected in Q4 2018; Three Rare Genetic Disease Programs Unveiled –

– Company in a Strong Financial Position to Launch TIBSOVO® (Ivosidenib) and Execute Research and Clinical Plans with Q1 2018 Ending Cash, Cash Equivalents and Marketable Securities of $995M –

CAMBRIDGE, Mass., May 4, 2018 — Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, is hosting an Investor Day in New York City today. During the event, the company will provide a comprehensive business update and report financial results for the first quarter ended March 31, 2018. The presentations will highlight how Agios' drug discovery platform and broad clinical portfolio set Agios on the path to become a sustainable, multi-product biopharmaceutical company. The event will be webcast today starting at 8:00 a.m. ET at investor.agios.com.

"As we prepare to launch our second Agios-discovered and first wholly owned medicine later this year, we continue to invest in our productive drug discovery engine and advance a robust pipeline of first-in-class medicines," said David Schenkein, M.D., chief executive officer at Agios. "Our first quarter progress against that objective was highlighted by the NDA acceptance of TIBSOVO® in IDH1m relapsed or refractory AML and multiple clinical trial initiations, including dosing the first patient with our MAT2A inhibitor AG-270 and the start of our AG-348 pivotal program in PK deficiency."

HIGHLIGHTS FROM INVESTOR DAY PRESENTATIONS

- Communicated a robust research pipeline consisting of nine advanced drug discovery programs against novel targets across oncology, rare genetic diseases and metabolic immuno-oncology with the potential to deliver multiple INDs over the next 24 months.
- Expanded rare genetic disease portfolio:
    - The company disclosed active research programs in three rare genetic diseases: phenylketonuria (PKU), erythroid porphyria and Friedreich's ataxia

- The most advanced research program is in PKU, where Agios has developed a novel approach to stabilize the mutant phenylalanine hydroxylase (PAH) protein and has demonstrated significantly decreased blood phenylalanine levels in a severe pre-clinical model of the disease. PKU is an autosomal recessive disease caused by mutations in the PAH gene affecting approximately 16,000 patients in the U.S.[1]

- Updated clinical milestones to advance the development of isocitrate dehydrogenase (IDH) 1 inhibitors in solid tumors:
  - Glioma pivotal development strategy expected to be finalized by year-end 2018
  - Completion of enrollment of ClarIDHy, a global, registration-enabling randomized Phase 3 study for ivosidenib in IDH1m positive advanced cholangiocarcinoma, accelerated to the first half of 2019
- Announced acceptance of the following presentations at 2018 American Society of Clinical Oncology (ASCO) Annual Meeting:
  - Updated data from the expansion phase of the ongoing Phase 1 study of ivosidenib in IDH1m relapsed or refractory (R/R) acute myeloid leukemia (AML)
  - Updated data from the ongoing Phase 1/2 combination trial of enasidenib or ivosidenib with VIDAZA® in patients with newly diagnosed AML with an IDH2 or IDH1 mutation ineligible for intensive chemotherapy
  - First clinical data from the Phase 1 study of AG-881 in advanced IDHm positive solid tumors, including glioma
- Completed commercial infrastructure build, including the deployment of an expanded sales force, to successfully launch TIBSOVO® (ivosidenib) within 48 hours of potential FDA approval.

FIRST QUARTER 2018 HIGHLIGHTS & RECENT PROGRESS

- Initiated ACTIVATE-T, a single-arm pivotal trial for AG-348, in adult pyruvate kinase (PK) deficiency patients who receive regular blood transfusions.
- Initiated PEAK, a global registry, for adult and pediatric patients with PK deficiency.
- Initiated a perioperative ‘window’ trial with ivosidenib and AG-881 in IDHm low-grade glioma to further investigate their effects on brain tumor tissue.
- Initiated a Phase 1 dose-escalation trial for AG-270, a first-in-class methionine adenosyltransferase 2a (MAT2A) inhibitor, in patients with methylthioadenosine phosphorylase (MTAP)-deleted tumors.
- Announced FDA acceptance, priority review and a Prescription Drug User Fee Act (PDUFA) action date of August 21, 2018 for the new drug application (NDA) for TIBSOVO® (ivosidenib) for the treatment of patients with R/R AML with an IDH1 mutation.
- Completed an underwritten public offering of 8,152,986 shares of common stock at the offering price of $67.00 per share, resulting in proceeds to the company, net of underwriting discounts and commissions, of approximately $516.2 million.

UPCOMING 2018 MILESTONES & EXPECTED DATA PRESENTATIONS

The company expects to achieve the following additional milestones in 2018:

Cancer:

- Potential approval and commercialization of TIBSOVO® (ivosidenib) in the United States for R/R AML with an IDH1 mutation in the third quarter of 2018.
- Submit a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for TIBSOVO® (ivosidenib) for the treatment of patients with R/R AML and an IDH1 mutation in the fourth quarter of 2018.
- Support, in collaboration with Celgene, the initiation of HO150, an intergroup sponsored, global, registration-enabling Phase 3 trial combining ivosidenib or enasidenib with standard induction and consolidation chemotherapy in frontline AML patients with an IDH1 or IDH2 mutation in the fourth quarter of 2018.
- Present updated data from the ongoing Phase 1 combination trial of enasidenib or ivosidenib with standard-of-care intensive chemotherapy in patients with newly diagnosed AML with an IDH2 or IDH1 mutation to the 2018 American Society of Hematology (ASH) Annual Meeting and Exposition.

Rare Genetic Diseases:

- Initiate ACTIVATE, a global, placebo-controlled, pivotal trial for AG-348 in approximately 80 adults with PK deficiency who do not receive regular blood transfusions in the second quarter of 2018.
- Initiate a Phase 2 proof of concept trial of AG-348 in thalassemia in the fourth quarter of 2018.

Research:

- Submit an investigational new drug (IND) application for our newest development candidate, AG-636, an inhibitor of the metabolic enzyme dihydroorotate dehydrogenase (DHODH) for the treatment of hematologic malignancies in the fourth quarter of 2018.

FIRST QUARTER 2018 FINANCIAL RESULTS & CASH GUIDANCE

Revenue for the quarter ended March 31, 2018 was $8.8 million, which includes $7.4 million of collaboration revenue and $1.4 million of royalty revenue from net sales of IDHIFA®. Revenue for the quarter ended March 31, 2017 was $10.5 million and consisted solely of collaboration revenue. The decrease in collaboration revenue recognized for the quarter ended March 31, 2018 compared to the comparable period in 2017 was primarily driven by adoption of the new revenue recognition standard.

Research and development (R&D) expenses were $78.2 million, including $8.6 million of stock-based compensation expense, for the quarter ended March 31, 2018, compared to $62.7 million, including $7.0 million in stock-based compensation expense, for the comparable period in 2017. The increase in R&D expense was primarily attributable to start-up costs for the AG-348 pivotal program in PK deficiency, including the initiation of the ACTIVATE-T trial. R&D expense also increased as a result of the initiation of a Phase 1 dose-escalation study of AG-270, our first-in-class MAT2A inhibitor, and IND enabling activities for AG-636, our DHODH inhibitor.

General and administrative (G&A) expenses were $24.6 million, including $5.9 million of stock-based compensation expense, for the quarter ended March 31, 2018, compared to $14.8 million, including $3.7 million of stock-based compensation expense, for the quarter ended March 31, 2017. The increase in G&A expense was primarily attributable to the growth in our U.S. commercial organization in order to support the expected launch of TIBSOVO® (ivosidenib) in the third quarter of 2018.

Net loss for the quarter ended March 31, 2018 was $90.8 million, compared to a net loss of $66.2 million for the quarter ended March 31, 2017.

Cash, cash equivalents and marketable securities as of March 31, 2018 were $994.7 million, compared to $567.8 million as of December 31, 2017. The increase in cash was driven by the net proceeds of $516.2 million from the January follow on offering, $4.4 million of cost reimbursements under our collaboration agreements with Celgene and $12.3 million received from employee stock transactions. This was offset by expenditures to fund operations of $104.8 million during the quarter ended March 31, 2018.

The company expects that its cash, cash equivalents and marketable securities as of March 31, 2018, together with the anticipated product and royalty revenue, anticipated interest income, and anticipated expense reimbursements, but excluding any additional program-specific milestone payments, will enable the company to fund its anticipated operating expenses and capital expenditure requirements through at least the end of 2020.

WEBCAST INFORMATION

The live webcast from today's event can be accessed under "Events & Presentations" in the Investors section of the company's website at www.agios.com. The archived webcast will be available on the company's website after the event.

About Agios

Agios is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic diseases through scientific leadership in the field of cellular metabolism. In addition to an active research and discovery pipeline across both therapeutic areas, Agios has an approved oncology precision medicine and multiple first-in-class investigational therapies in

clinical and/or preclinical development. All Agios programs focus on genetically identified patient populations, leveraging our knowledge of metabolism, biology and genomics. For more information, please visit the company's website at www.agios.com.

About Agios/Celgene Collaboration

IDHIFA® (enasidenib) and AG-881 are part of Agios' global strategic collaboration with Celgene Corporation focused on cancer metabolism. Under the terms of the 2010 collaboration agreement, Celgene has worldwide development and commercialization rights for IDHIFA®. Agios continues to conduct certain clinical development activities within the IDHIFA® development program and is eligible to receive reimbursement for those development activities and up to $95 million in remaining payments assuming achievement of certain milestones, and royalties on any net sales. Celgene and Agios are currently co-commercializing IDHIFA® in the U.S. Celgene will reimburse Agios for costs incurred for its co-commercialization efforts. For AG-881, the companies have a joint worldwide development and 50/50 profit share collaboration, and Agios is eligible to receive regulatory milestone payments of up to $70 million. AG-270 is part of a 2016 global research collaboration agreement with Celgene. Through Phase 1 dose escalation, Celgene has the option, for a fee of at least $30 million, to participate in a worldwide cost and profit share with Agios. Upon exercise of the option the parties will share all development costs, subject to specified exceptions, and any profits on net sales and Agios will be eligible for up to $169 million in clinical and regulatory milestone payments for the program.

Cautionary Note Regarding Forward-Looking Statements

This press release contains 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® (ivosidenib), AG-881, 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 collaborator, Celgene, 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 press release 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 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 press release 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.

Consolidated Balance Sheet Data
(in thousands)
(Unaudited)

	March 31, 2018	December 31, 2017
Cash, cash equivalents and marketable securities	$ 994,747	$ 567,750
Collaboration receivable – related party	3,512	2,448
Royalty receivable – related party	1,417	1,222
Total assets	1,040,126	614,397
Deferred revenue – related party	121,043	163,640
Stockholders' equity	865,594	375,503

Consolidated Statements of Operations Data
(in thousands, except share and per share data)
(Unaudited)

	Three Months Ended March 31, 2018	2017
Collaboration revenue – related party	$ 7,345	$ 10,508
Royalty revenue – related party	1,417	—
Total Revenue	8,762	10,508
Operating expenses:		
Research and development, net	78,224	62,732
General and administrative	24,550	14,823
Total operating expenses	102,774	77,555
Loss from operations	(94,012)	(67,047)
Interest income	3,187	881
Net loss	$ (90,825)	$ (66,166)
Net loss per share – basic and diluted	$ (1.63)	$ (1.56)
Weighted-average number of common shares used in computing net loss per share – basic and diluted	55,694,603	42,280,525

# # #

[1] National PKU Alliance, www.npkua.org

Investors:

Renee Leck, 617-649-8299
Senior Manager, Investor Relations
Renee.Leck@agios.com

Media:

Holly Manning, 617-844-6630
Associate Director, Corporate Communications
Holly.Manning@agios.com

Opening Remarks

David Schenkein, M.D., Chief Executive Officer

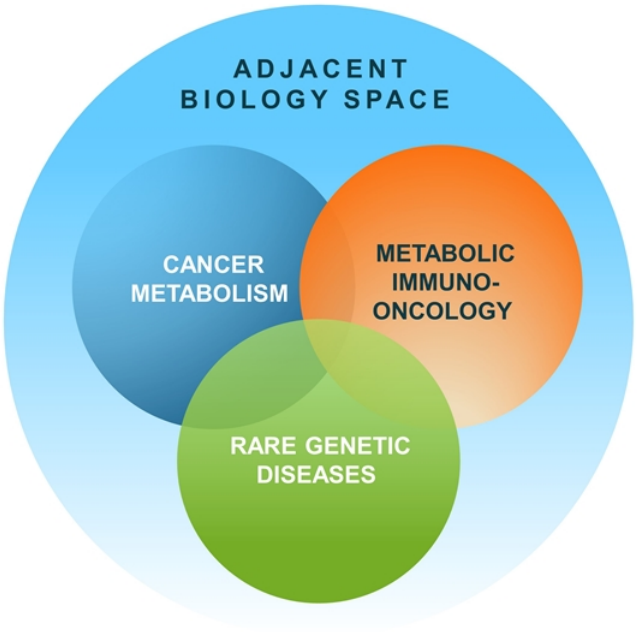
Forward Looking Statements

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® (ivosidenib), AG-881, 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," "estimate," "expect," "intend," "may," "plan," "predict," "prepare," "project," "would," "could," "potential," "possible," "hope," "strategy," "milestone," "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 collaborator, Celgene, 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 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 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 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.

Today's Agenda

Time	Speaker
8:00 - 8:15 a.m.	Opening Remarks – **David Schenkein, M.D.,** Chief Executive Officer
Research	
8:15 - 9:00 a.m.	Discovery Strategy & Research Portfolio – **Scott Biller, Ph.D**., Chief Scientific Officer & **Kevin Marks, Ph.D.,** Senior Director, Head of Cancer Biology
9:00 - 9:20 a.m.	Q&A Part 1
Clinical Development, Commercial & Finance	
9:20 - 10:00 a.m.	Ivosidenib Clinical & Commercial Strategy in Acute Myeloid Leukemia – **Darrin Miles**, Vice President, IDH Program Management & **Steve Hoerter**, Chief Commercial Officer
10:00 - 10:30 a.m.	Opportunity for IDH1 Inhibition in Solid Tumors – **Susan Pandya, M.D.,** Senior Medical Director, Clinical Development & **Maeve Lowery, M.B., B.Ch., B.A.O.,** Trinity College Dublin
10:30 - 11:00 a.m.	AG-348 Clinical Development in Pyruvate Kinase Deficiency & Rare Hemolytic Anemias – **Chris Bowden, M.D.,** Chief Medical Officer
11:00 - 11:15 a.m.	Financial Overview & Q1 Results – **Andrew Hirsch,** Chief Financial Officer & Head of Corporate Development
11:15 - 12:00 p.m.	Q&A Part 2 & Buffet Lunch

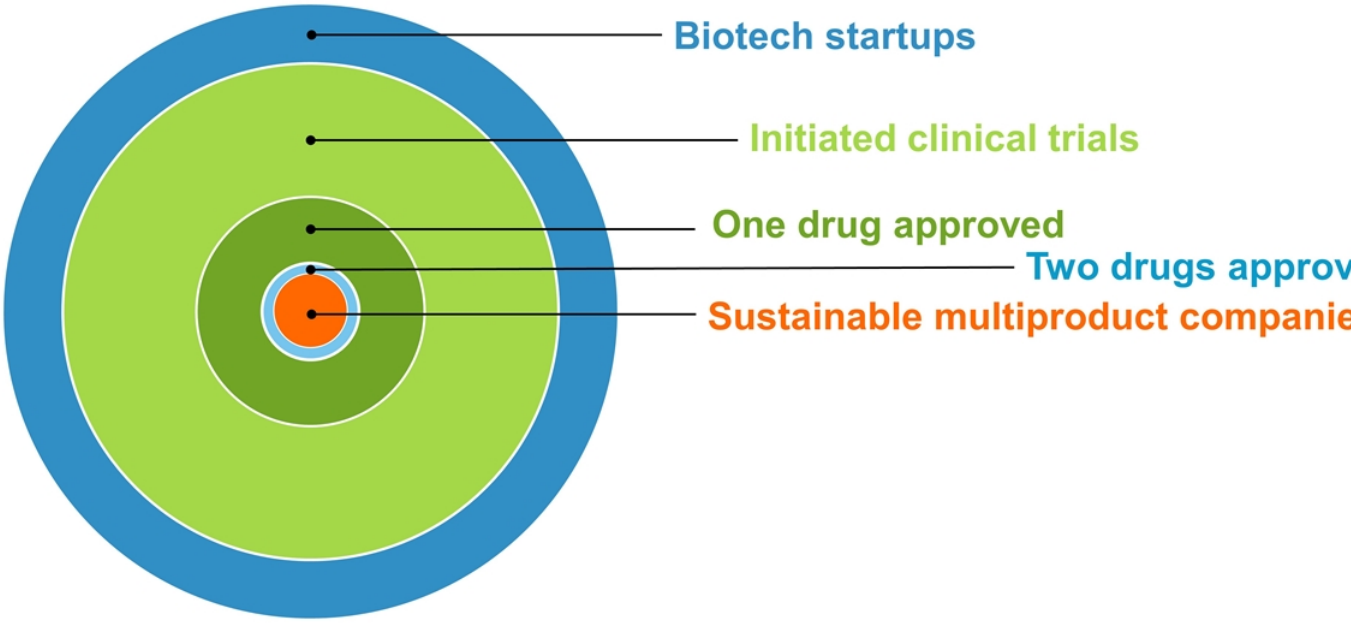
Driven By a Clear Vision and Values



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



Agios' Scientific Platform Demonstrates Remarkable, Reproducible Productivity

DISCOVERY

$50-60M
INVESTED IN DRUG DISCOVERY ANNUALLY

SCIENCE

40+
PEER-REVIEWED PUBLICATIONS

CULTURE

400+ EMPLOYEE

1 VISION

10+
CLINICAL TRIALS IN **6** DISEASES

1,000+
PATIENTS TREATED IN CLINICAL TRIALS

6 INDs

1ST MEDICINE APPROVED **+2ND** NDA ACCEPTED **+3** ADDITIONAL COMPOUNDS IN CLINICAL DEVELOPMENT

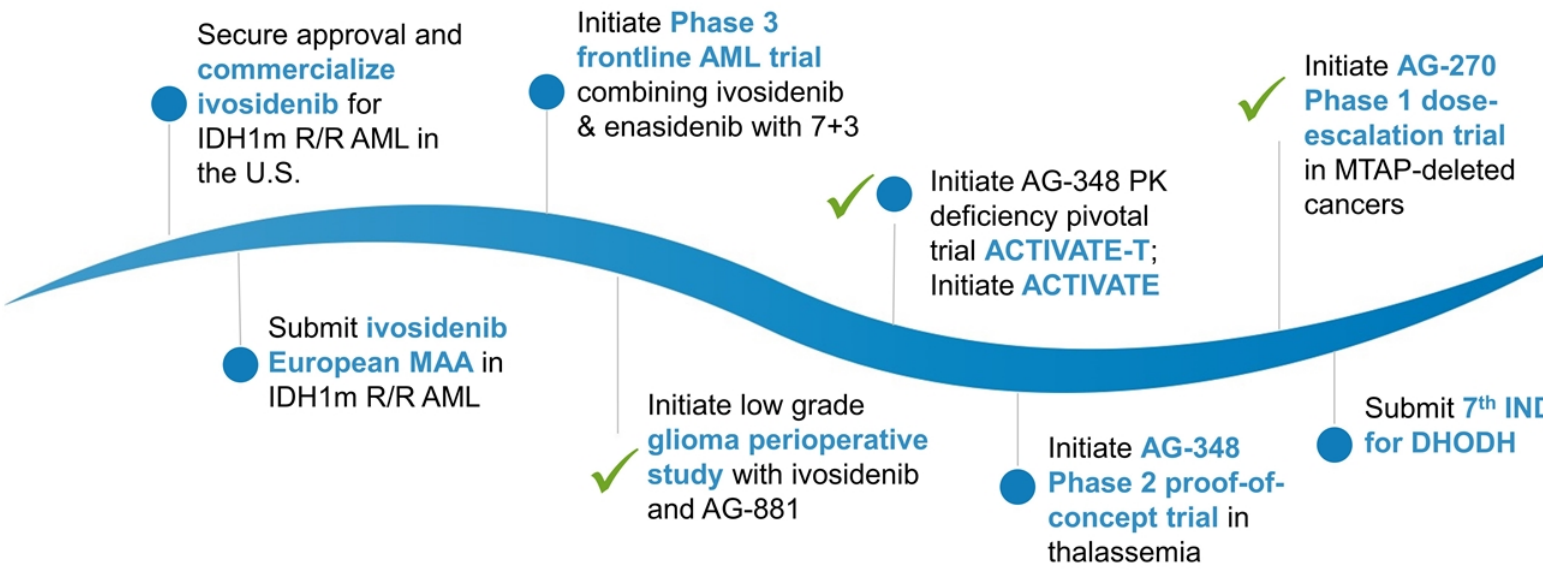
IN 4 YEARS SINCE FIRST PATIENT DOSED

Current Clinical Portfolio Has Potential to Benefit Large Number of Patients

ACUTE MYELOID LEUKEMIA	~10,000 IDHm Patients AML Opportunity ~$2B
CHOLANGIO-CARCINOMA	~3,000 IDH1m Patients
PYRUVATE KINASE DEFICIENCY	~3,000 to ~8,000 Patients
LOW GRADE GLIOMA	~9,000 IDH1m 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



2018 Goals Set Stage for Building Long-Term Value

2018 GOALS

- Secure approval and commercialize ivosidenib for R/R AML in the U.S.
- Initiate Phase 3 frontline AML trial combining ivosidenib & enasidenib with 7+3
- ✓ Initiate AG-348 PK deficiency pivotal trial (ACTIVATE-T)
- ✓ Initiate AG-270 Phase 1 dose-escalation trial
- Submit ivosidenib European MAA
- ✓ Initiate glioma perioperative study
- Initiate AG-348 Phase 2 trial in thalassemia
- Submit 7th IND for DHODH

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			●		
Ivosidenib (IDH1m Inhibitor)	R/R AML			● NDA accepted		agios
	Frontline AML			●		
	Cholangio			●		
	Glioma		●			
AG-881 (pan-IDHm Inhibitor)	Glioma		●			agios Celgene
AG-348 (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

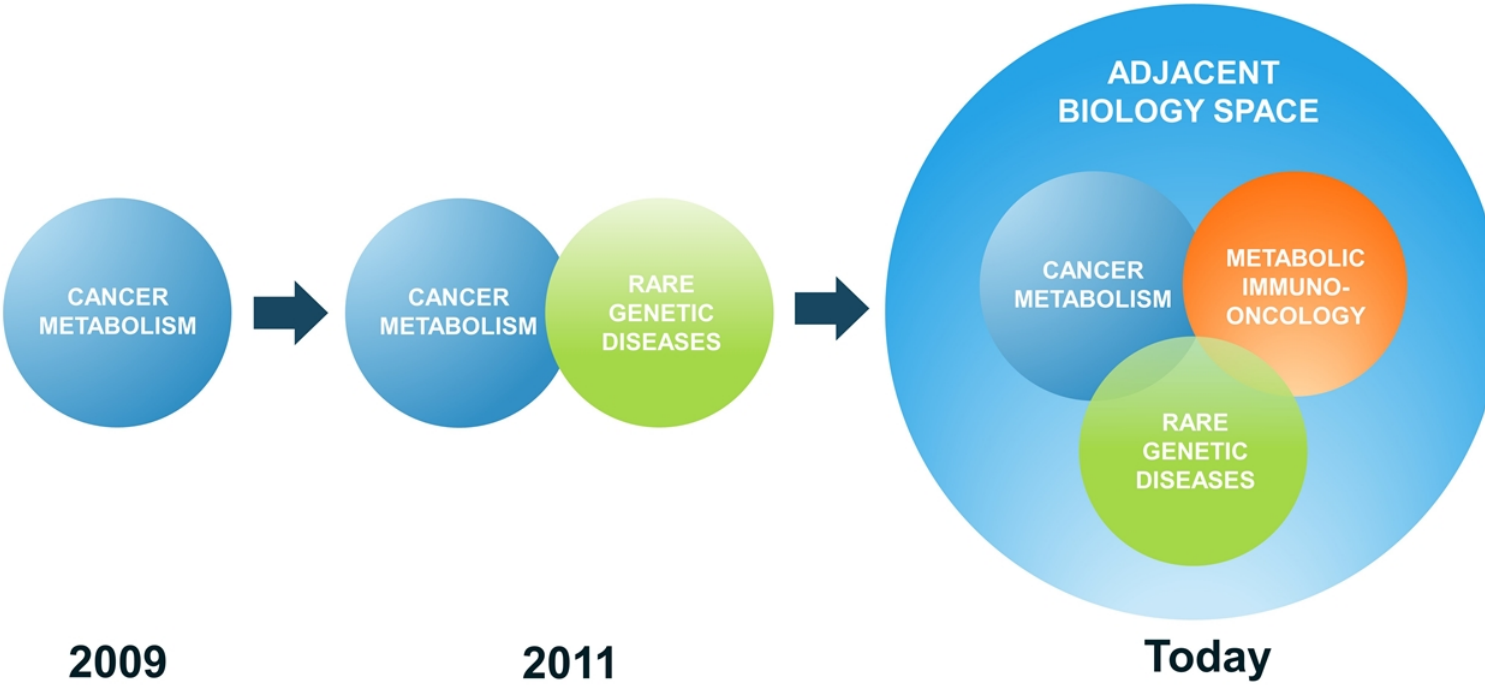
What You Will Hear and See Today

- Research engine poised to deliver next wave of development candidates
  - Several new programs highlighted
  - 9 programs currently in advanced drug discovery
- Robust clinical development plans in place across our early and late-stage programs
- Ready to launch our 2nd commercial product
- Well capitalized to execute on our business plan
- Culture focused on science and patient impact

Discovery Strategy & Research Portfolio

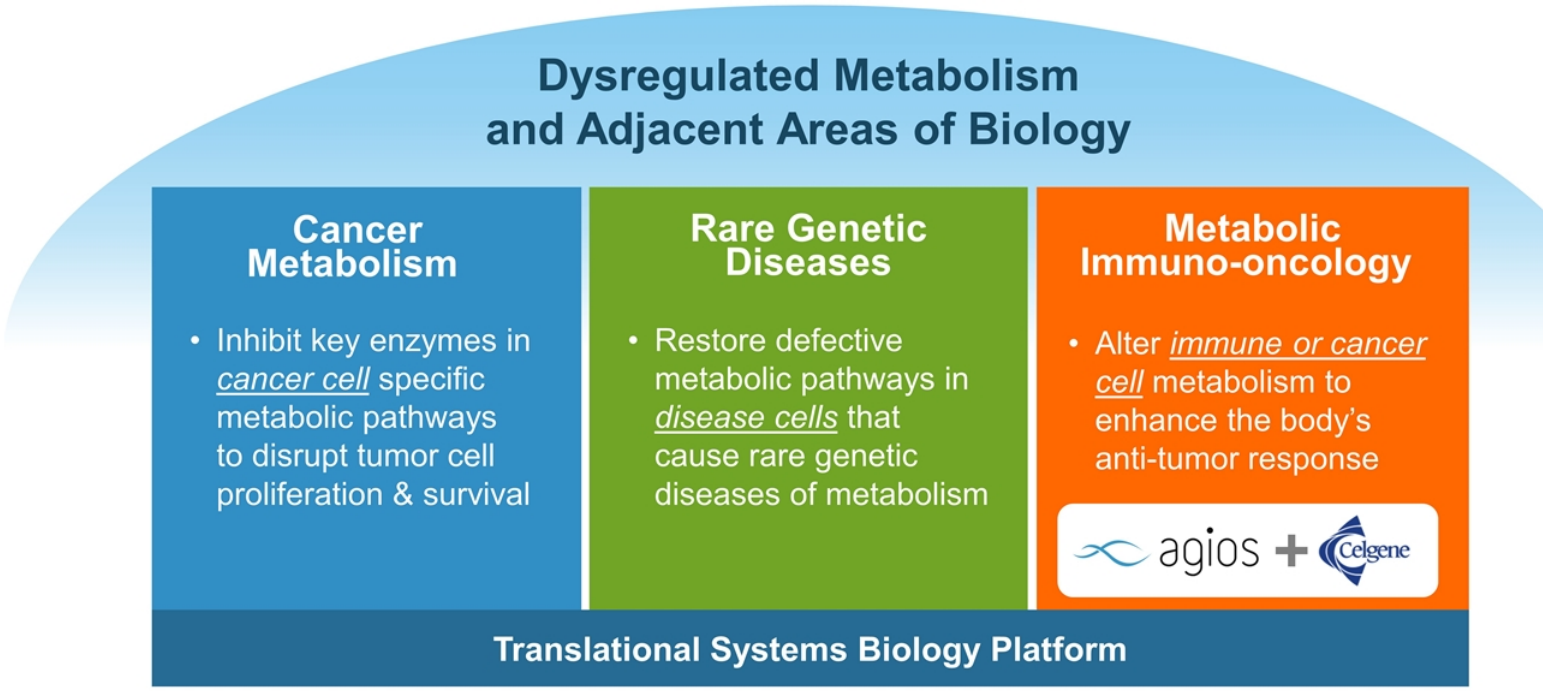
Scott Biller, Ph.D., Chief Scientific Officer

Evolving the Agios Research Portfolio Into Adjacent Biologic Areas



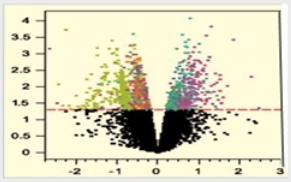
2009 **2011** **Today**

Agios Research Focus



Evolving our Technology Platform from our Historic Strength in Metabolism to a Cutting-Edge, Systems Biology Approach

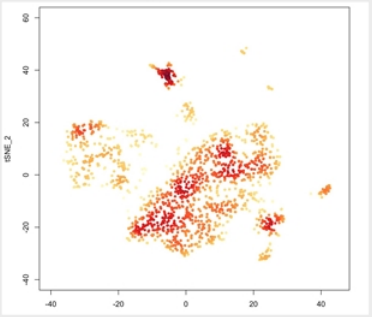
Metabolomics + Informatics + Modeling



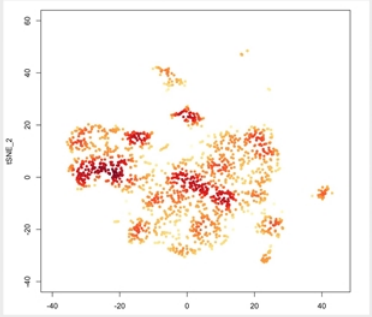
Multi-Omics + Imaging + Data Integration → New Knowledge

Single Cell RNA Sequencing

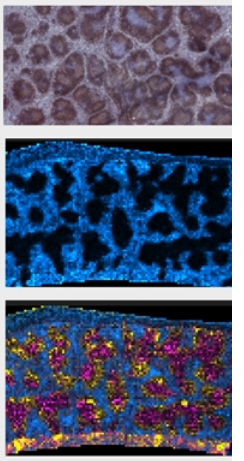
Day 5 Drug



Day 5 Vehicle



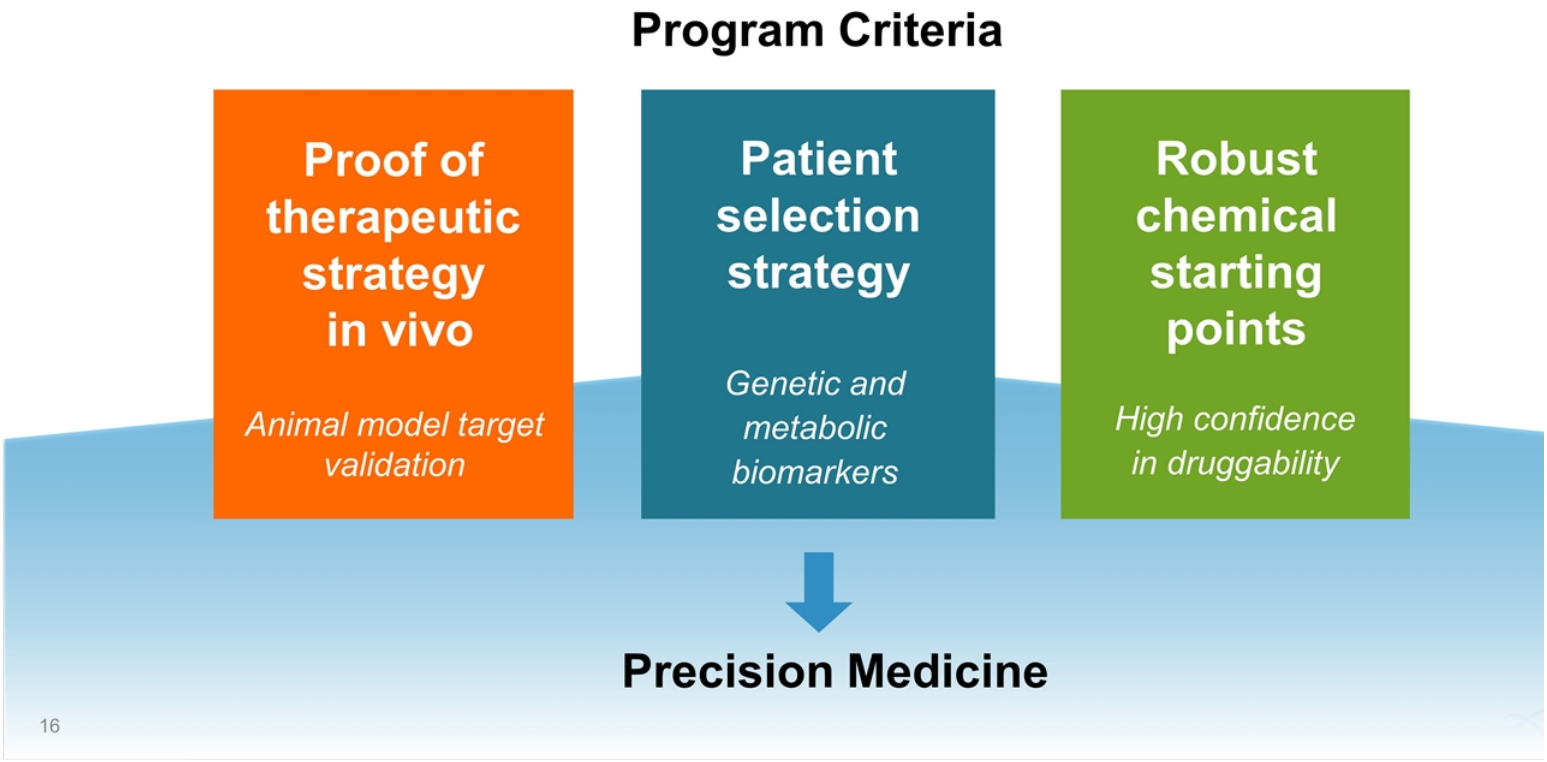
Tissue Imaging



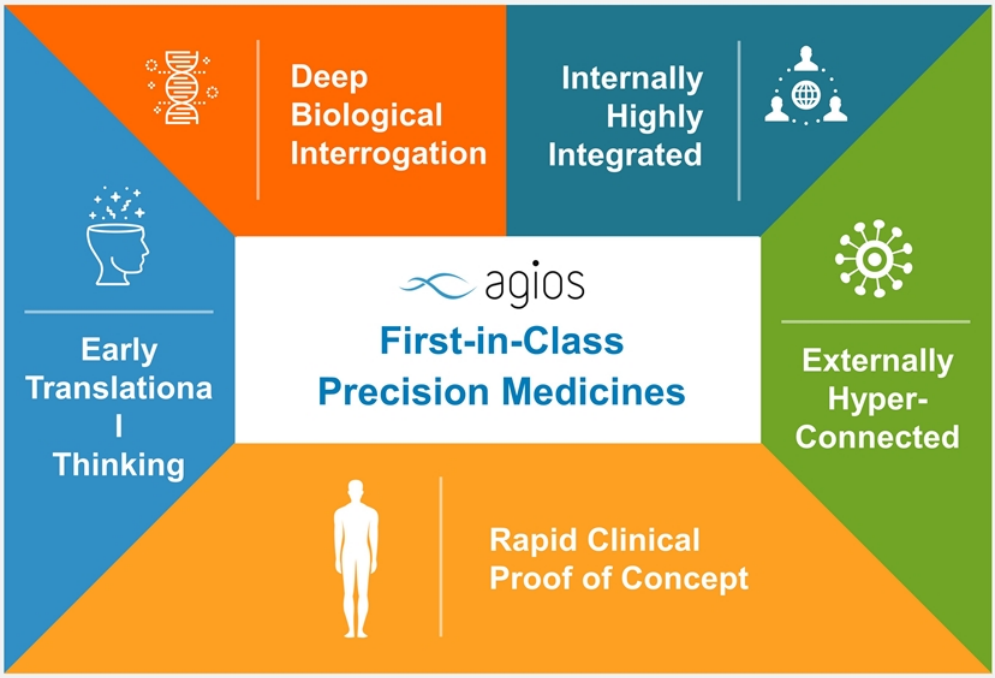
Deep understanding of biology with a translational focus

Source: Agios data on file

High Probability of Success for Agios Drug Discovery



What Differentiates Agios Research Strategy?

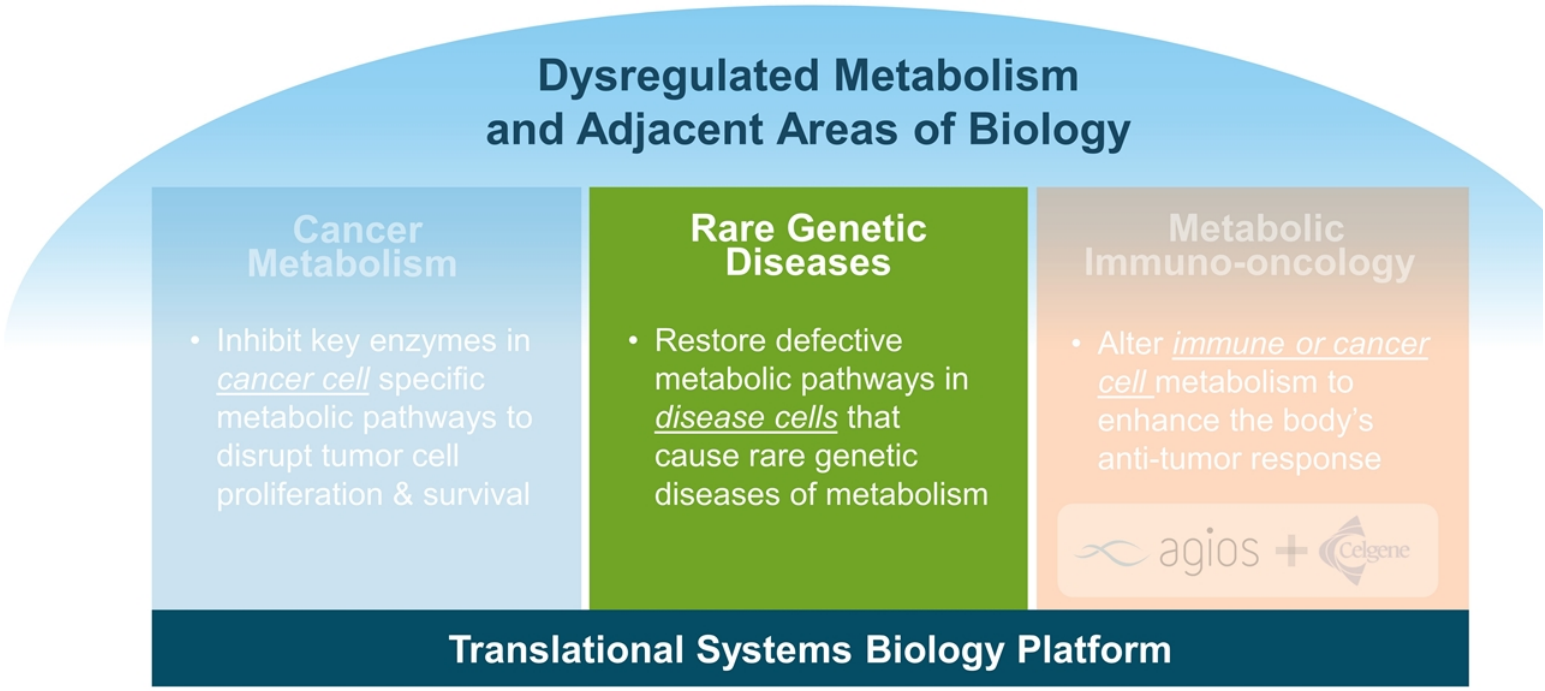


Agios Preclinical Pipeline

Program	Target Discovery	Target Validation	Drug Discovery	Drug Candidate
Oncology				
Heme Lineage: AG-636 DHODH				●
MAT2A Follow-Ons			●	
Genetically Defined Heme Target			●	
Genetically Defined Solid Tumor 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)	●			

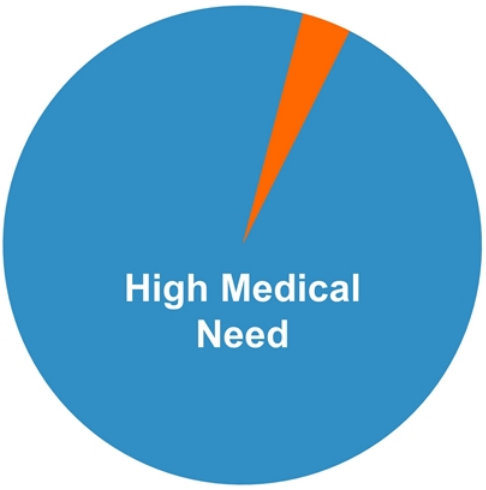
● Metabolic Target ● Non-Metabolic Target ◐ Metabolic and Non-Metabolic Targets ▬ Celgene Collaboration

Agios Areas of Research Focus

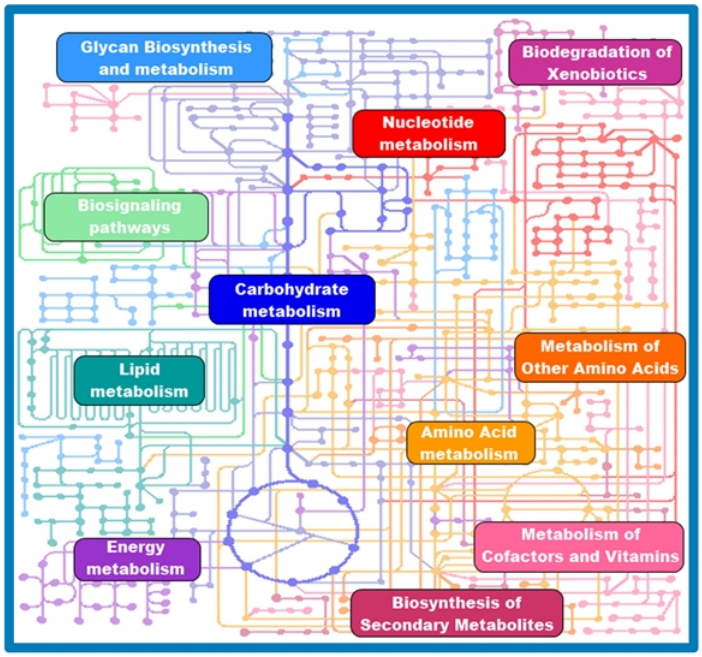


Expanding the Playing Field in Rare Genetic Diseases (RGD)

~5% of Rare Diseases have approved drugs

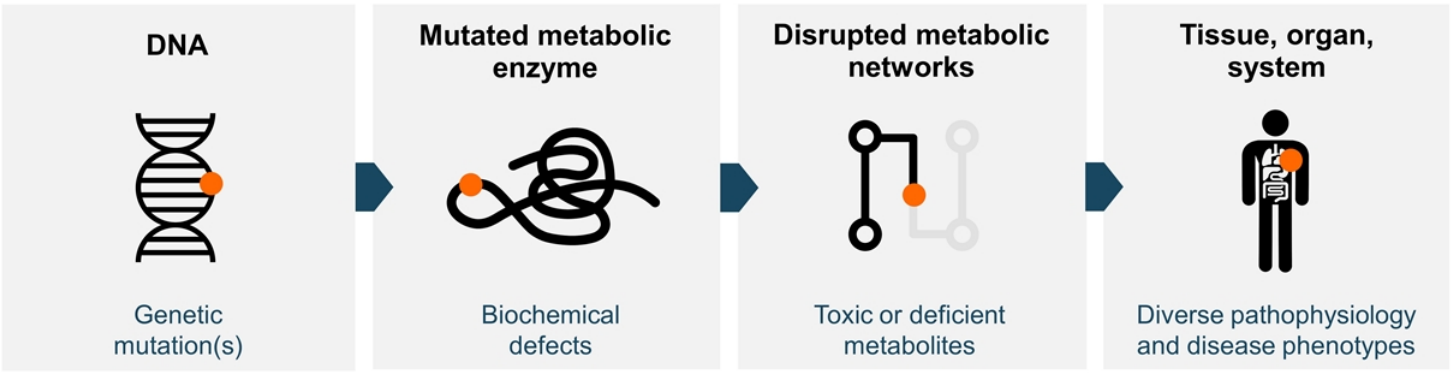


~500 Rare Diseases of Metabolism

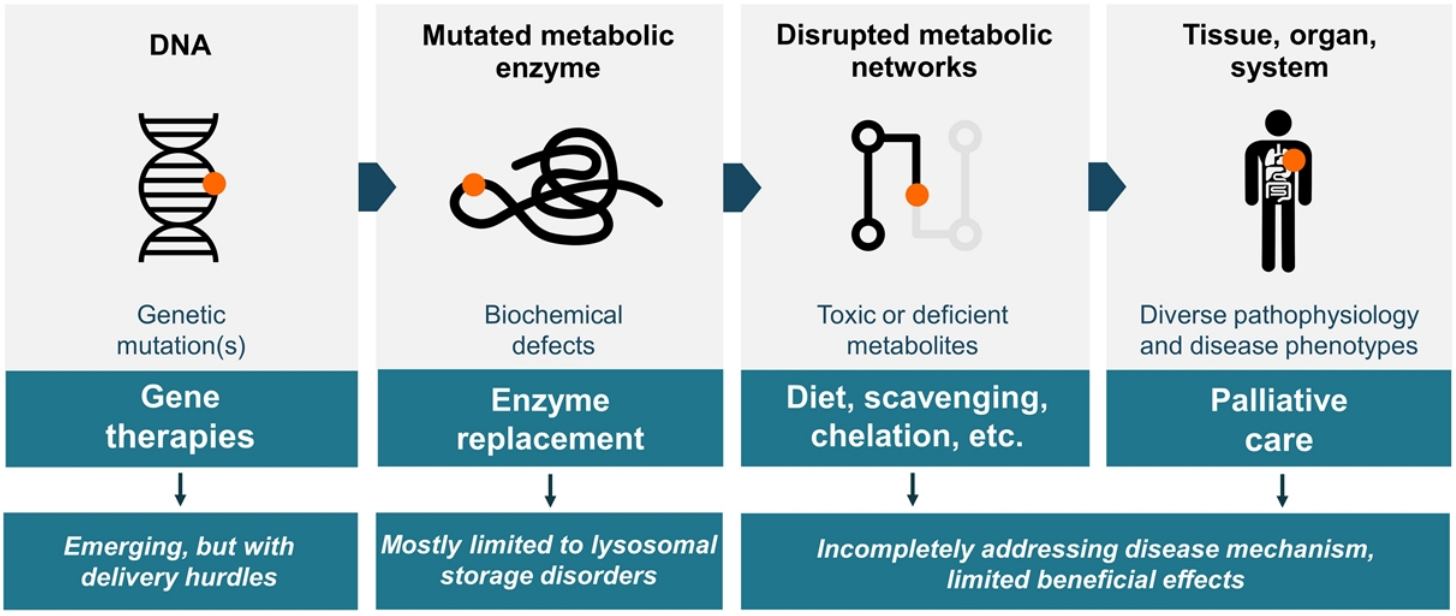


Sources: http://rarediseaseday.us/; https://rarediseases.info.nih.gov/diseases/diseases-by-category/14/metabolic-disorders; http://150.214.214.5/metabolicpathways/

Rare Genetic Disease Pathogenesis



The Current Therapeutic Landscape



Creating a New Wave of Transformational Therapies

Understanding and correcting the root cause of the disease

DNA	Mutated metabolic enzyme	Disrupted metabolic networks	Tissue, organ, system
			
Genetic mutation(s)	Biochemical defects	Toxic or deficient metabolites	Diverse pathophysiology and disease phenotypes

Agios Approach

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

Agios RGD Disease Selection Attributes

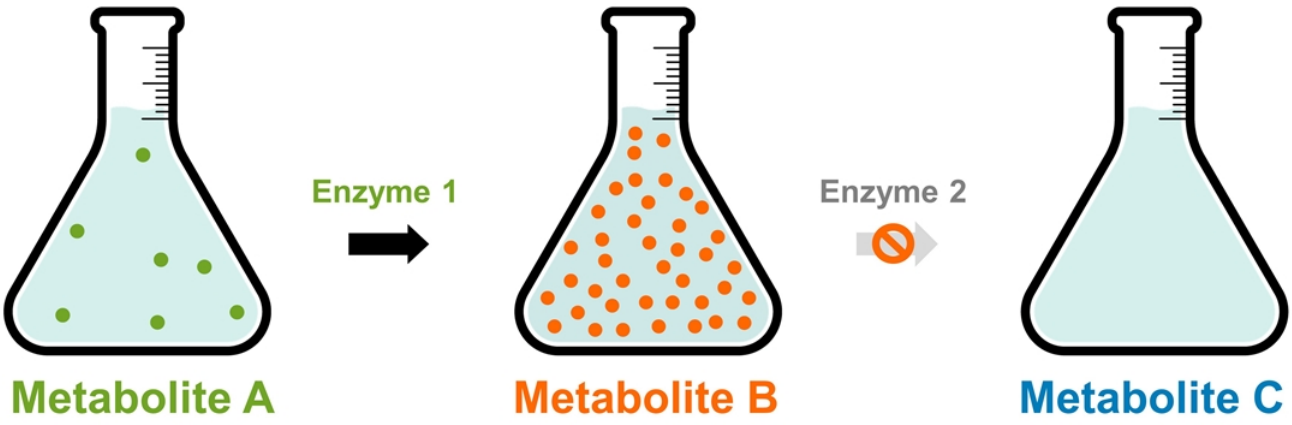
Disease Selection Criteria and Differentiated Therapeutic Strategies

Defining Novel Therapeutic Strategies:
Agios' Competitive Advantage

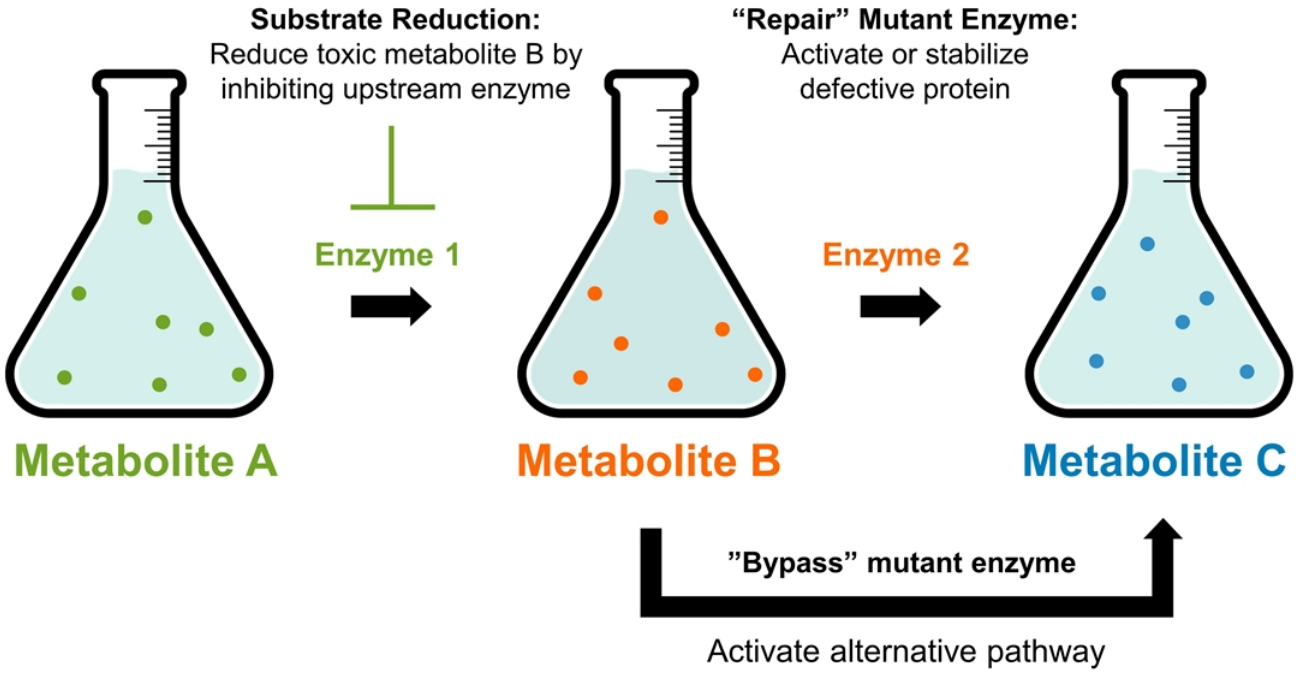
Effective Intervention Strategy

- Develop deep insight into mechanism of disease pathophysiology
- Validate therapeutic strategies in disease models
  - Patient derived cell models and genetically engineered animal models
- Design small molecule drugs using a combination of all-available technologies
- Discover pharmacodynamic and mechanistic biomarkers for rapid proof-of-concept in humans

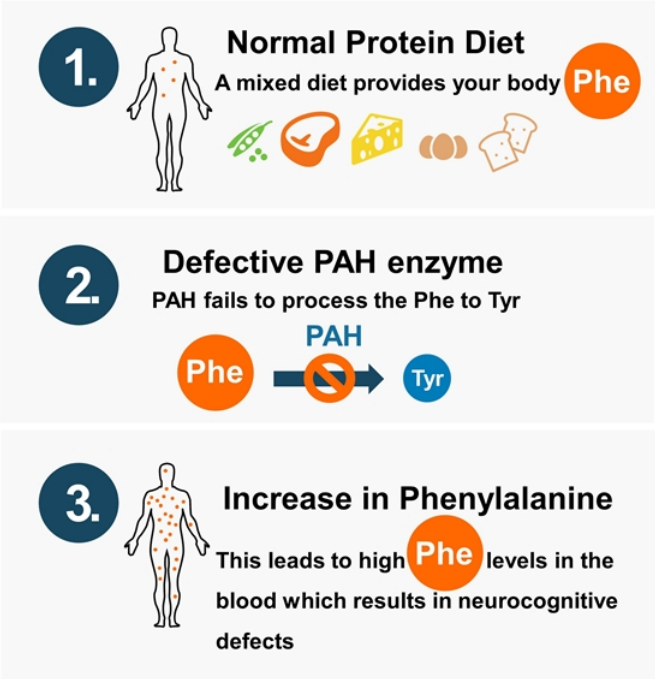
Small Molecule Strategies to Correct Disease Pathology



Small Molecule Strategies to Correct Disease Pathology



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



- ~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'

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

1. Normal Protein Diet

A mixed diet provides your body Phe

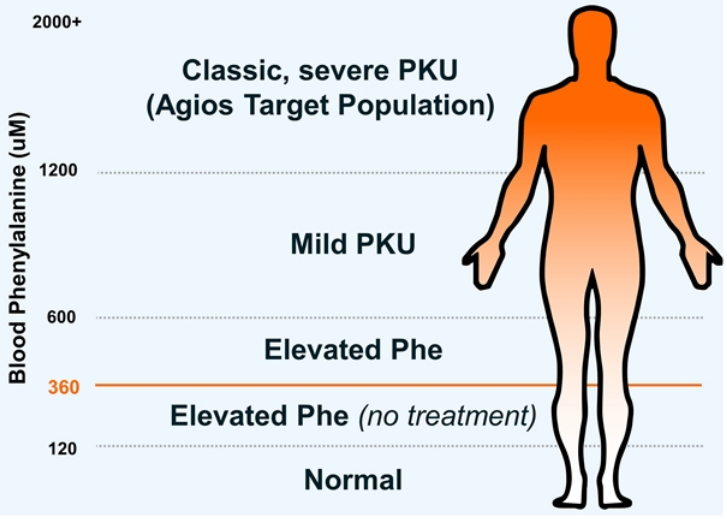
2. Defective PAH enzyme

PAH fails to process the Phe to Tyr

Phe → PAH → Tyr

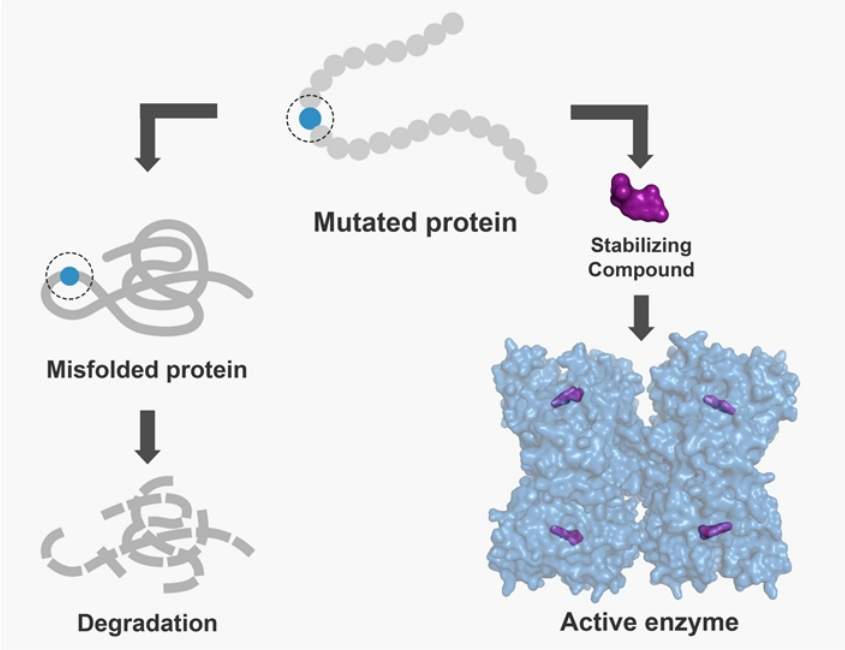
3. Increase in Phenylalanine

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



Severity of disease correlates with extent of phenylalanine elevation Phe

Therapeutic Strategy: Stabilize Mutant PAH to Rescue Enzyme Activity



> 900 different mutations found in PAH

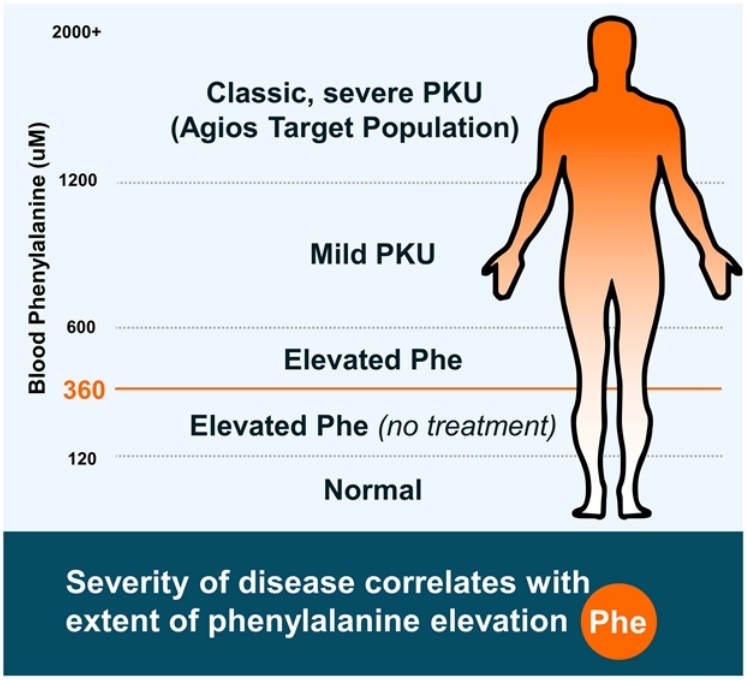
Majority result in misfolded protein leading to degradation

Agios approach is to stabilize mutant PAH

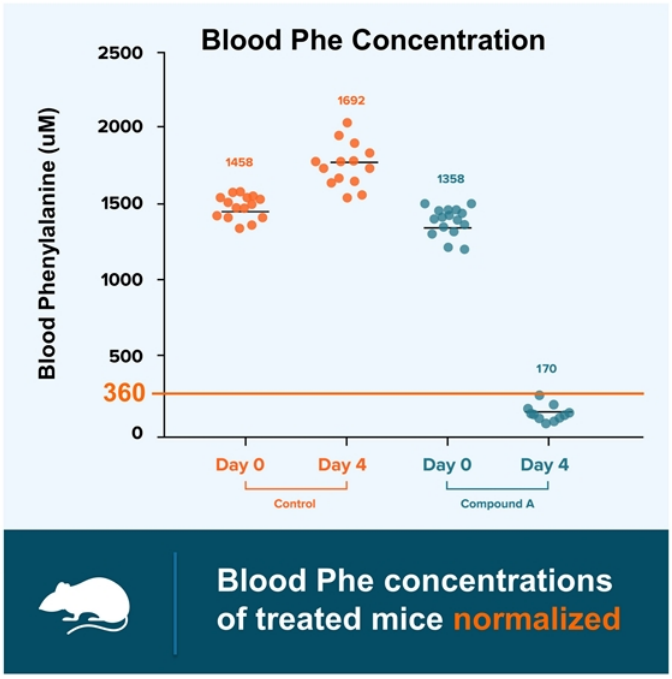
Stabilization leads to increase in active protein levels, leading to lower Phe levels

Source: PAHvdb (http://www.biopku.org/pah/); www.BIOPKU.org; https://www.ncbi.nlm.nih.gov/books/NBK1504/

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



Severity of disease correlates with extent of phenylalanine elevation Phe

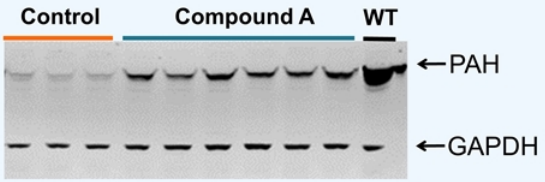


Blood Phe concentrations of treated mice normalized

Source: Agios data on file

Agios Lead Molecule Increases PAH Protein Levels in the Liver of Severe PKU Mouse

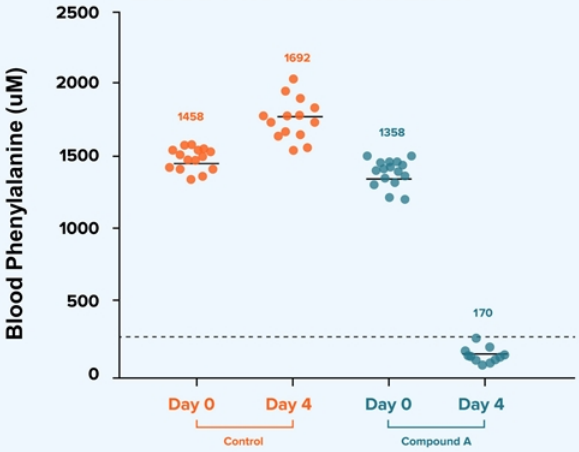
Stabilization of mutant PAH protein in knock-in mouse model of severe PKU



Western blot, 6 hours after final dose

PAH protein levels in livers of treated mice increased

Blood Phe concentration



Blood Phe concentrations of treated mice normalized

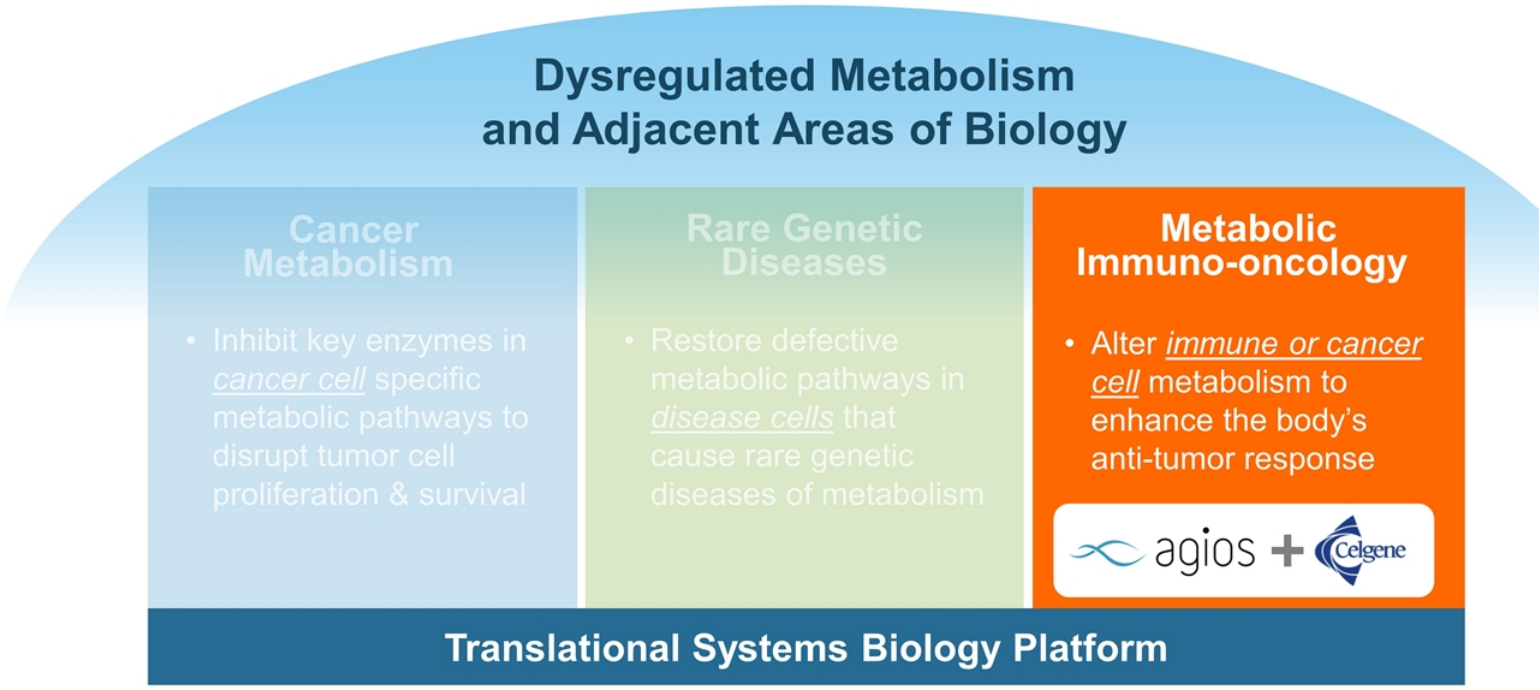
Source: Agios data on file

Emerging Portfolio of First-in-Class RGD Programs

Program	Target Discovery	Target Validation	Drug Discovery	Development Candidate
Pyruvate Kinase Activator Follow-Ons			●	
Phenylketonuria			●	
Erythroid Porphyria			●	
Friedreich's Ataxia			●	
Exploratory (Multiple Diseases)	◐	◐		

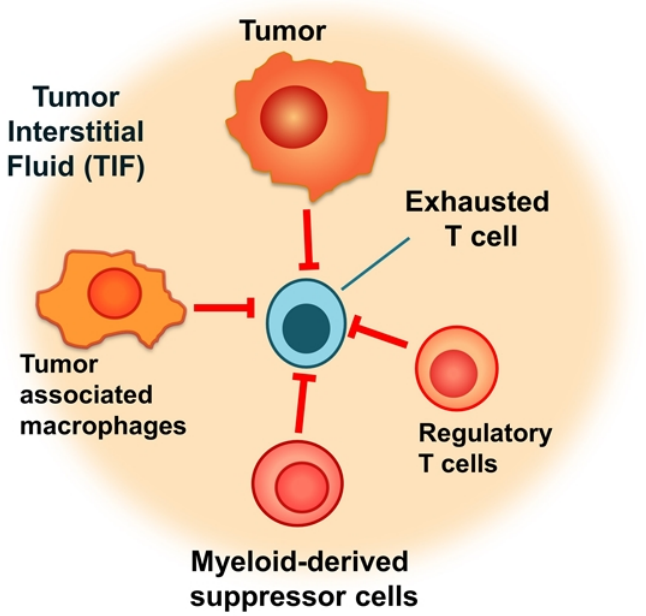
● Metabolic Target ● Non-Metabolic Target ◐ Metabolic and Non-Metabolic Targets

Agios Areas of Research Focus



Metabolic Immuno-Oncology (IO)

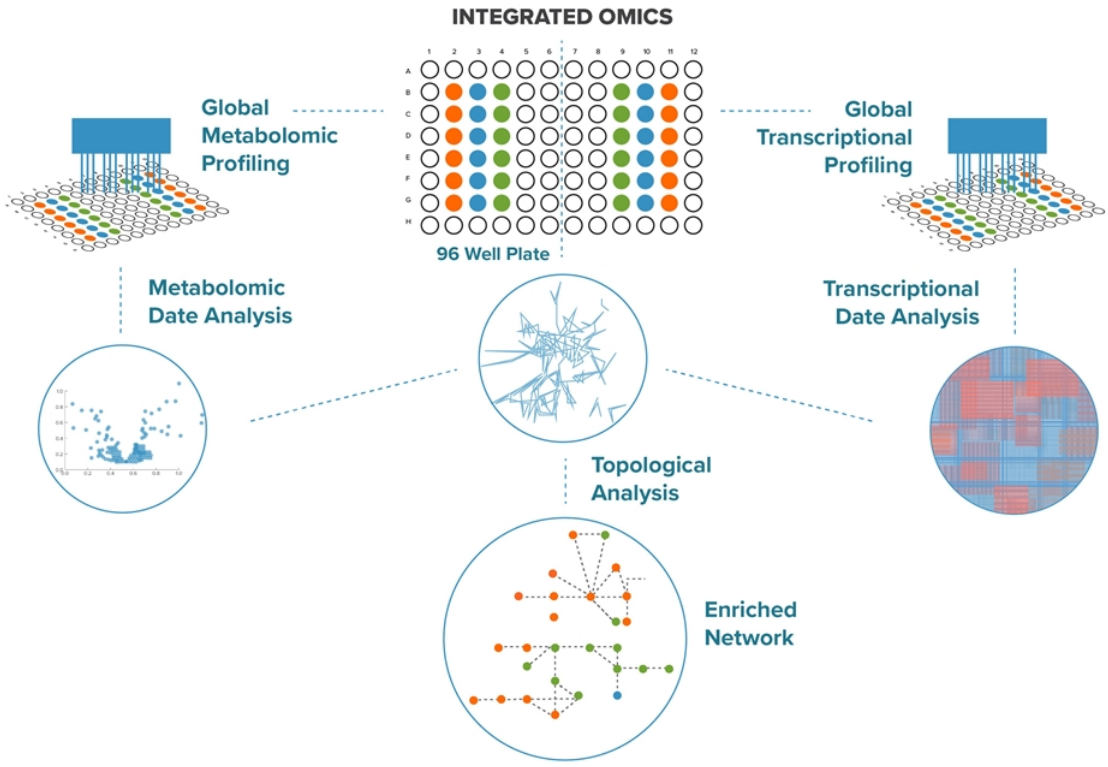
Immunosuppressive Tumor Microenvironment



Agios Metabolic IO Strategy

- Discover targets with potential for single agent activity
- Increase response rates by utilizing patient selection strategies
- Identify mechanism based combination therapies

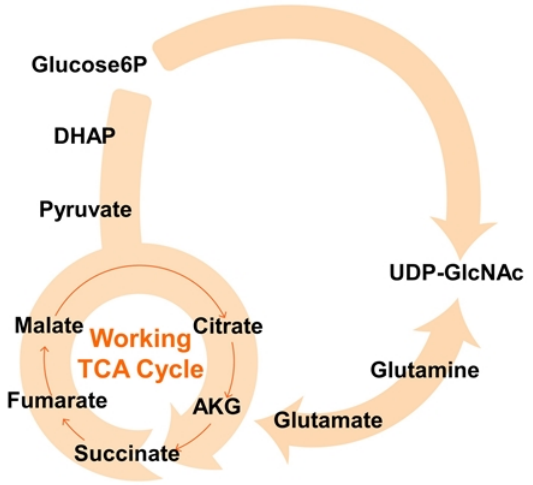
Integrated Metabolomics and Gene Expression Profiling



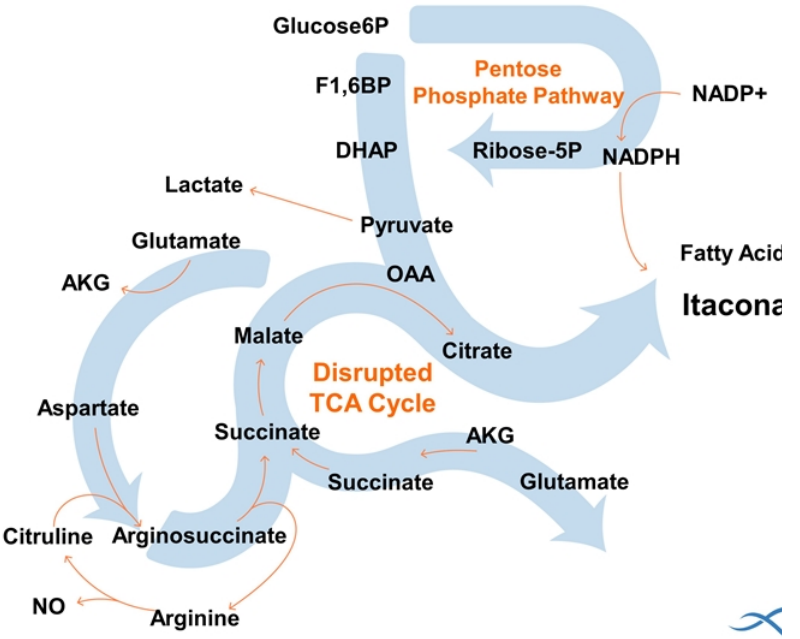
Source: Agios collaboration with the Artyomov Lab, Washington University St. Louis / Immunity Journal March 2015, Volume 42 Issue 3

Inflammatory and Immunosuppressive Macrophages Have Dramatically Different Metabolic Programs

Immunosuppressive Macrophage



Inflammatory Macrophage



Source: Immunity Journal March 2015, Volume 42 Issue 3

Building a Comprehensive Translational Platform to Deeply Interrogate the Tumor Microenvironment

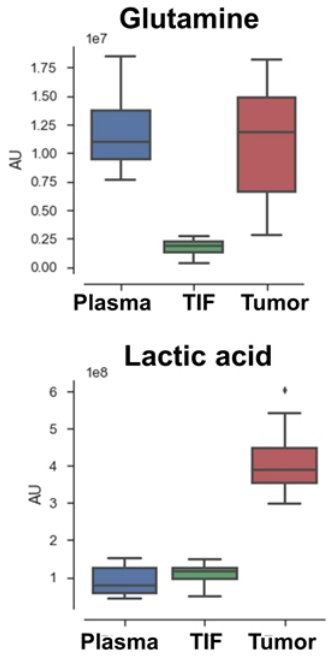
Whole Tissue Analysis	Single Cell Analysis	Whole Tissue Imaging

Understanding the tumor microenvironment in mouse models and human tumors to:

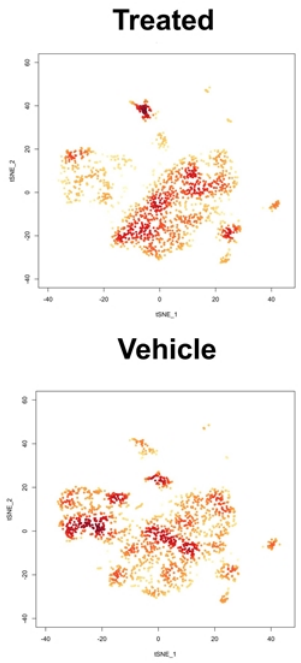
- Uncover novel therapeutic mechanisms
- Discover new strategies for patient stratification

Building a Comprehensive Translational Platform to Deeply Interrogate the Tumor Microenvironment

Tumor Interstitial Fluid

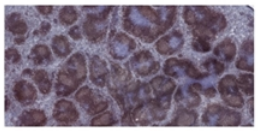


Single Cell Analysis

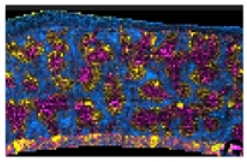


Whole Tissue Imaging

Tissue Architecture



MALDI Mass Spectroscopic Imaging



Pink = T-Cell metabolite
Yellow = B-Cell metabolite
Blue = Macrophage metabolite

Source: Agios data on file

Building a Network of Collaborators on Novel Targets and Technologies

Ongoing collaborations with 16 leading investigators in immunology and metabolism

McGill

- In vivo immune cell metabolism & T cell exhaustion

Washington University in St. Louis

- Metabolomic analysis of MCA tumor microenvironment

UNIVERSITY OF TORONTO

- Identification of cancer-cell intrinsic immunotherapy targets


Universiteit Leiden

NWO awards funding for LACDR research project to develop novel engineering approaches to study cancer immunity

22 December 2017

As part of the HTSM2017 funding program, the LACDR division for Systems Biomedicine and Pharmacology received 1.08 million euros for a research project to develop novel engineering approaches to fight cancer.

These approaches will enable diagnosis and characterization of cancer immunity at an unprecedented resolution and will be employed to develop individualized treatment strategies.

The project will be led by LACDR researchers Alireza Mashaghi and Thomas Hankemeier, in collaboration with Ron Heeren from Maastricht University. The work will be done in close collaboration with several industrial partners including Agios Pharmaceuticals (Boston), which are heavily involved in anti-cancer therapeutics and, in particular, cancer immunotherapy.

Agios Pharmaceuticals

Collaboration Structure:

- 1.1 MM € total matching grant from NWO
- Collaboration between Agios, Leiden University and Maastricht University

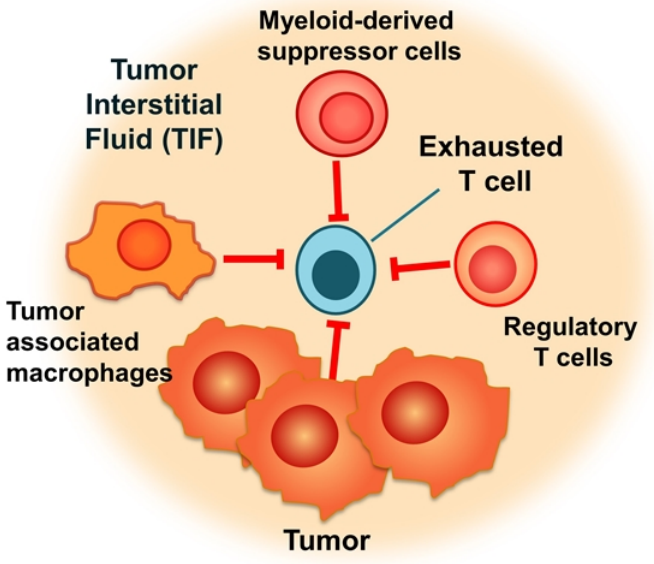
High resolution metabolic analysis of immune cells

- Development of an ultrasensitive robotic platform
- 3D cell culture screening techniques for high throughput screening of T-cells
- Single cell resolution of metabolites and tracers in cells with MS imaging

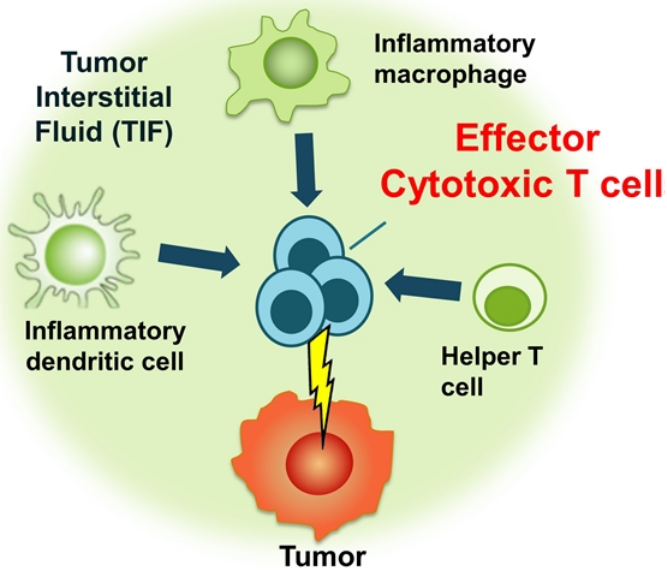
NWO is The Netherlands Organization for Scientific Research

A Growing Portfolio of Metabolic Strategies to Activate Immune Cell Killing of Tumor Cells

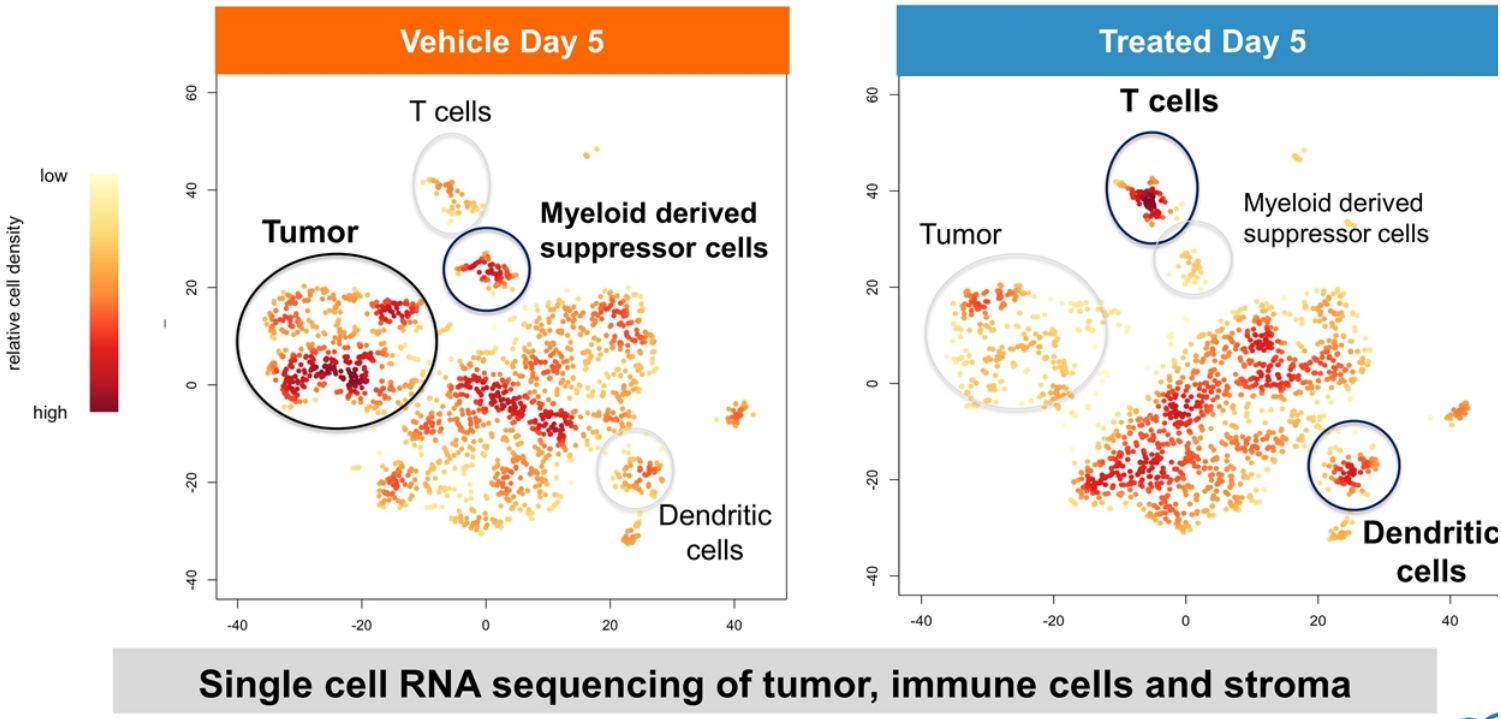
Immunosuppressive Tumor Microenvironment



Activation of Tumor Cell Killing by the Immune System



Inhibitor of Agios Macrophage Target Shows Predicted Immunomodulation and Antitumor Efficacy



Single cell RNA sequencing of tumor, immune cells and stroma

 Source: Agios data on file

Developing Metabolic Immuno-Oncology Pipeline

Program	Target Discovery	Target Validation	Drug Discovery	Drug Candidate
Metabolic Immuno-Oncology				
T-cell and Tumor Target			●	
Macrophage Target			●	
Macrophage Target		●		
Tumor Target		●		
Other Targets (T-cell, Macrophage, Tumor)	●	●		

● Metabolic Target Celgene Collaboration

Oncology Research Portfolio

Kevin Marks, Ph.D., Senior Director, Head of Cancer Biology

Multiple Paths to Precision Medicines in Oncology

Clearly Defined Patient Populations

Genetic Target

Target genetically altered

- Gain-of-function mutations
- Fusions
- Amplification

Example: **mutant IDH**

Genetic Context

Synthetic lethal with an oncogene or tumor suppressor

Synthetic lethal with a passenger gene deletion

Example: **MAT2A**

Lineage

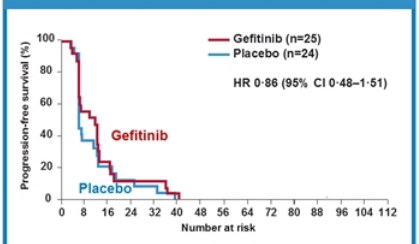
Lineage-specific dependency

Example: **DHODH**

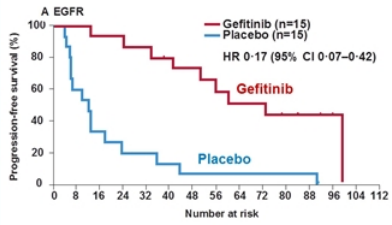
Precision Medicine in Cancer Metabolism

Directly drugging gain-of-function (GOF) mutants has yielded transformative medicines

EGFR WT NSCLC Patients

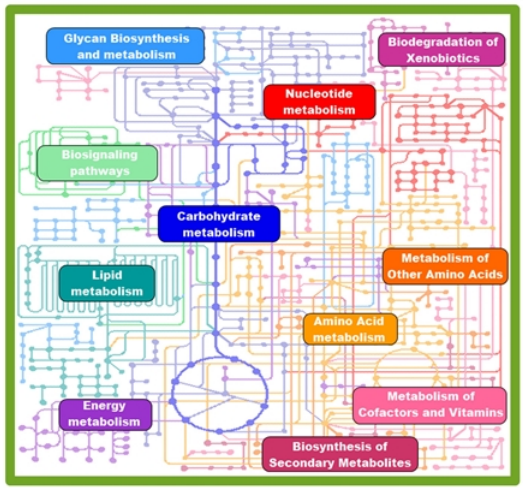


EGFR Mutant NSCLC Patients



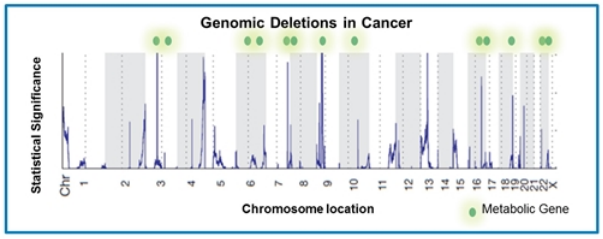
Source: Zhang, et al, Lancet Oncology, 2012

But, despite deep sequencing of many tumor types, IDH1/2 remain the only metabolic GOF mutations

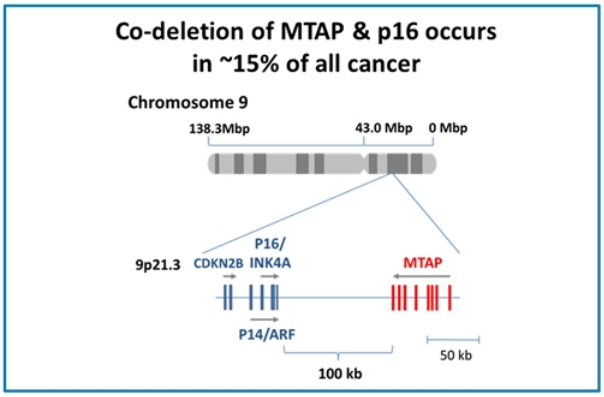


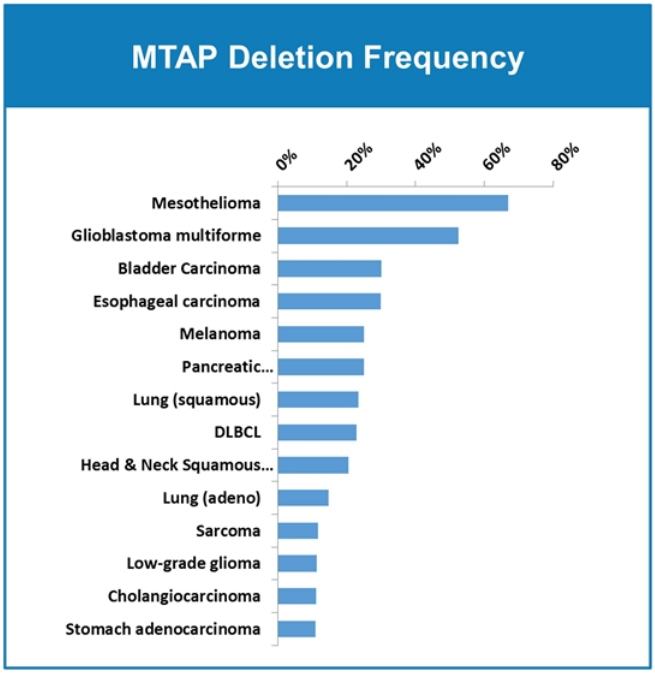
IDH1/2m

While Gain-of-Function Driver Mutations Are Scarce, Loss-of-Function Mutations Are Common



Source: Adapted from Beroukhim et al Nature 2010

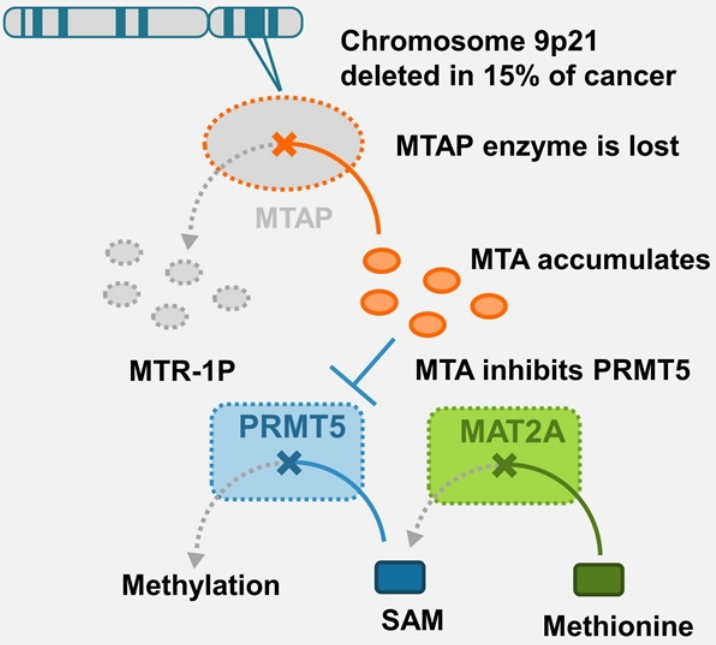




Sources: Marjon et al Cell Reports. 2016 Apr 19;15(3):574-587; Agios data on file; Illei et al Clinical Cancer Research. 2003 Jun; 9(6):2108-13; MTAP deletion frequencies are from Agios analysis of data from The Cancer Genome Atlas

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**

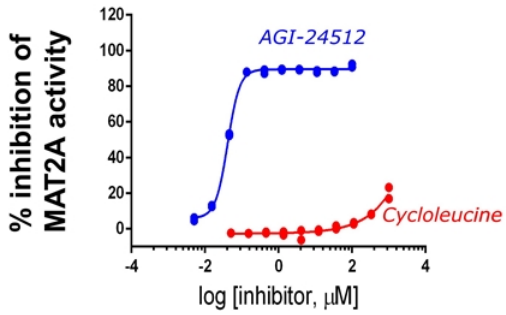


Sources: Marjon et al Cell Reports. 2016 Apr 19;15(3):574-587 and MTAP deletion frequency from Agios analysis of data from The Cancer Genome Atlas

Discovery of First in Class MAT2A Inhibitors and Validation of the MAT2A/MTAP Hypothesis

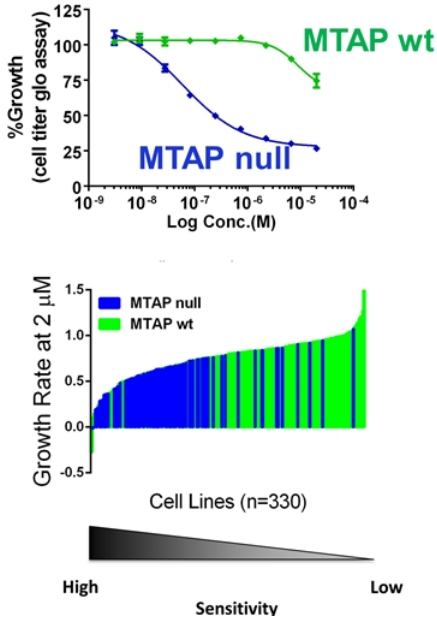
Identification of MAT2A Inhibitors

In vitro biochemical assay



MTAP-selective Growth Inhibition

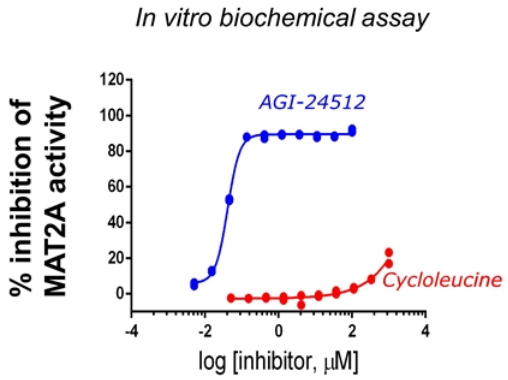
Growth Inhibition in Cancer Cells +/- MTAP



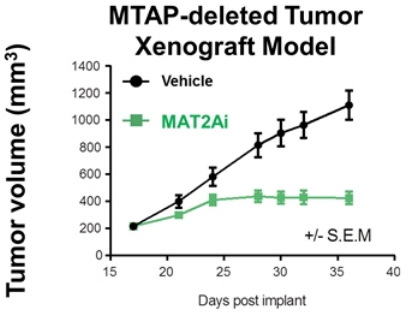
Source: Agios data on file

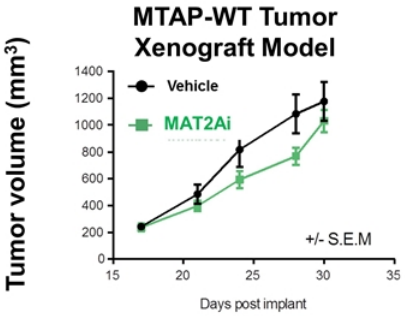
Discovery of First in Class MAT2A Inhibitors and Validation of the MAT2A/MTAP Hypothesis

Identification of MAT2A Inhibitors



MTAP-selective Growth Inhibition

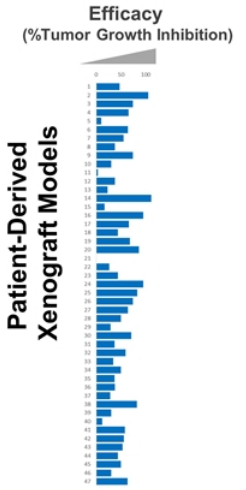




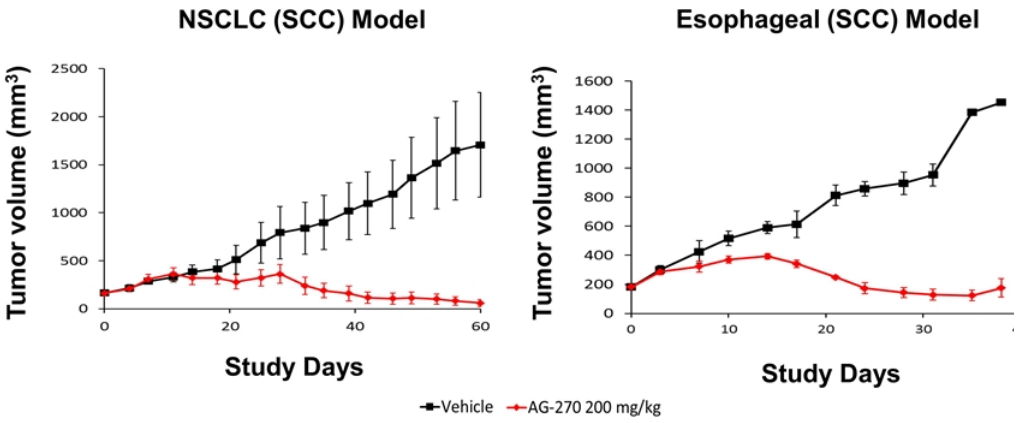
Source: Agios data on file

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

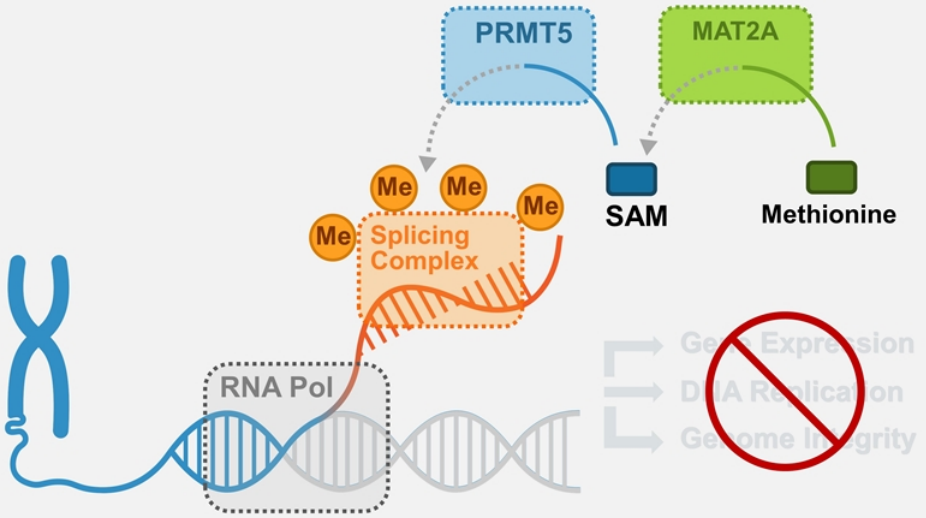


AG-270 is efficacious in MTAP-deleted PDX models from a variety of tissue origins including NSCLC, pancreatic, gastric & esophageal

Source: Agios data on file

Emerging Mechanistic Understanding of the Pathway Downstream of MAT2A

1. **RNA splicing concurrent with transcription**
2. **Splicing complex requires PRMT5**
3. **MAT2A inhibition blocks splicing**
4. **Defects in gene expression, DNA replication, genome integrity**



Source: Data presented at 2018 AACR Conference

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

Multiple Pharmacodynamic Biomarkers

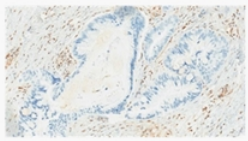
PATHWAY EFFECTS	CLINICALLY APPLICABLE BIOMARKERS
MAT2A inhibition	
↓ Tumor-selective inhibition of PRMT5	Monitor SAM in patient plasma
↓ Inhibition of PRMT5 targets including the spliceosome	Measure PRMT5 methyl marks in tumor
↓ Antiproliferative & cytotoxic effects	Assess splicing using RNA seq & other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

Patient Selection Biomarkers

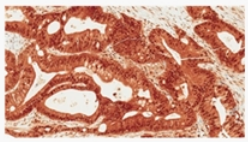
1. Next-gen sequencing for CDKN2A loss

2. Directly assess MTAP-status by IHC

MTAP deficient PDAC

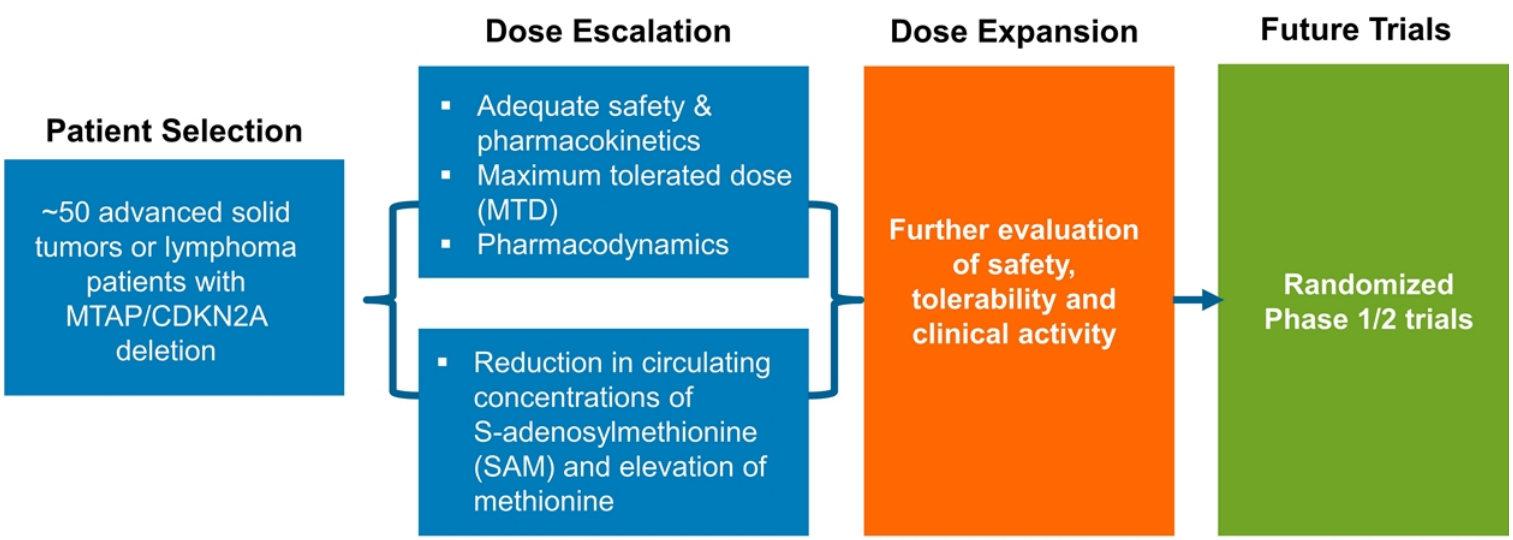


MTAP positive PDAC



Source: Agios data on file

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



ClinicalTrials.gov Identifier: NCT0

Trial initiated and enrolling patients

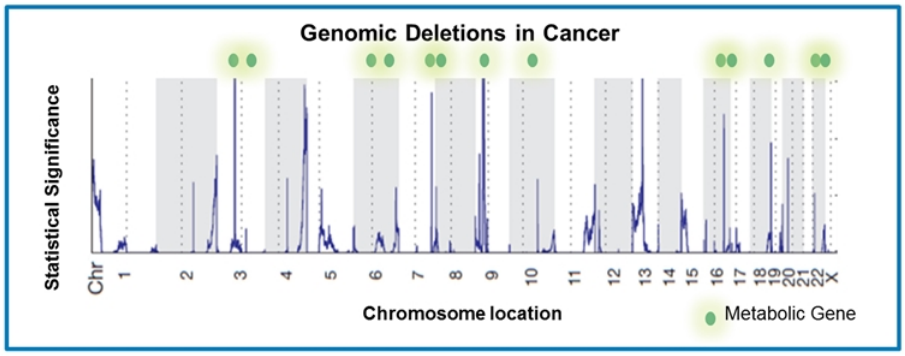
Systematically Searching for Other MAT2A/MTAP-like Programs

Datamining of human tumor data

Prevalent deletions with significant unmet need

CRISPR/shRNA screening platform

Custom bioinformatics to identify best target/genotype pairs



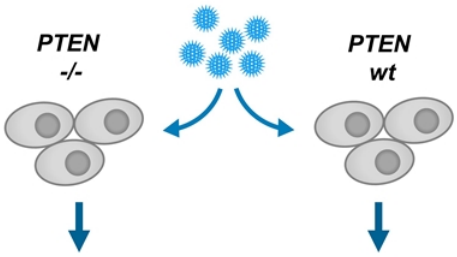
Source: Adapted from Beroukhim et al Natu

Agios' oncology research team systematically searching for vulnerabilities associated with many other major deletions in cancer

Next Wave Target Example: Novel Selective Vulnerability Target for PTEN-mutant Cancers

Internally identified target with robust target validation in vitro and in vivo

PTEN-selective functional genomics (shRNA) screen

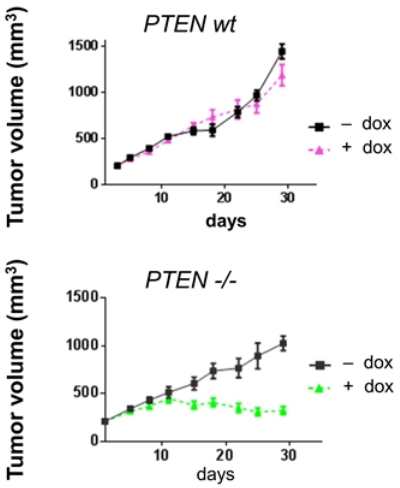


Measure shRNA depletion via RNA-seq of barcodes

$$\frac{PTEN\ -/-}{PTEN\ wt} = \text{Preferential depletion with } PTEN \text{ loss}$$

Successful validation of Target X

* PTEN-selective growth phenotypes upon dox-inducible knockdown of Target X *in vivo*



Source: Agios data on file

Multiple Paths to Precision Medicines in Oncology

Clearly Defined Patient Populations

Genetic target

Target genetically altered

- gain-of-function mutations
- fusions
- Amplification

Example: **mutant IDH**

Genetic context

Synthetic lethal with an oncogene or tumor suppressor

Synthetic lethal with a passenger gene deletion

Example: **MAT2A**

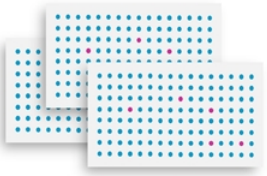
Lineage

Lineage-specific dependency

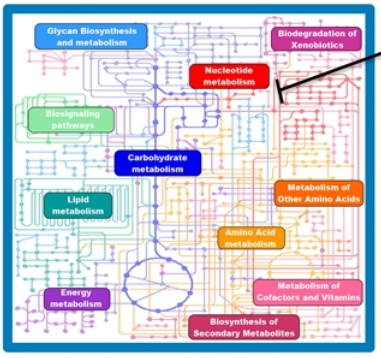
Example: **DHODH**

A Chemical Biology Screen Revealed an Unexpected Lineage Dependence on DHODH

Cell line panel screen reveals selective AG-636 sensitivity in heme malignancies

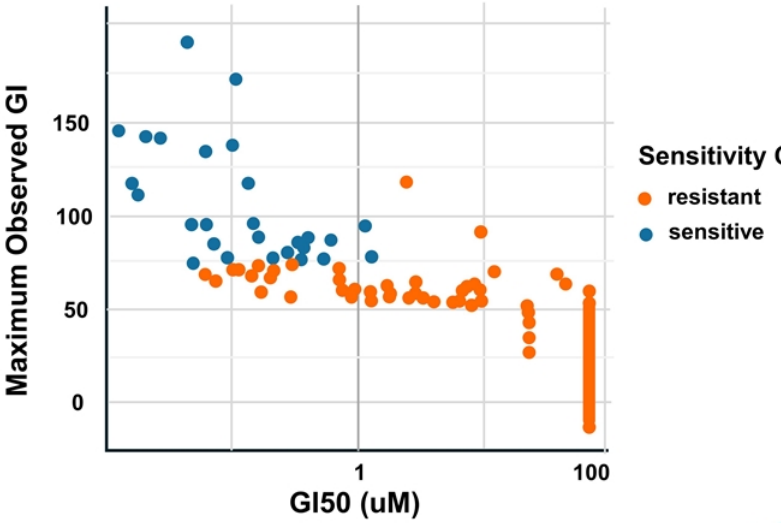


We tested a library of inhibitors of metabolic enzymes vs 100s of cancer cell lines, searching for selective agents



DHODH inhibitor AG-636 blocks production of nucleotides for RNA & DNA

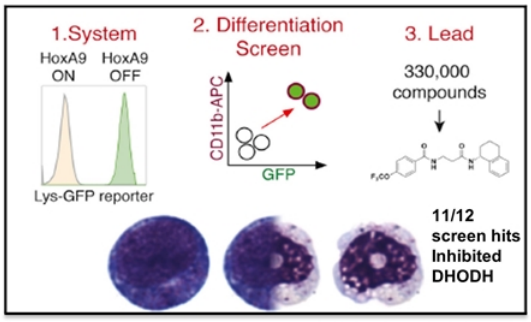
Selective efficacy:
AG-636 active in 8% of cancer cell lines (n=356)



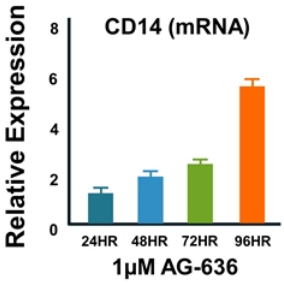
Source: Agios data on file

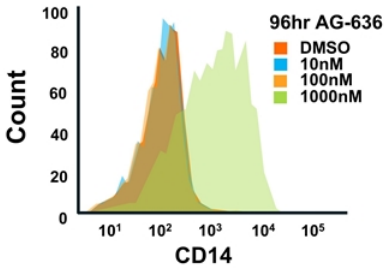
DHODH Inhibitor AG-636 is Efficacious in AML

Inhibition of DHODH overcomes differentiation blockade in AML…

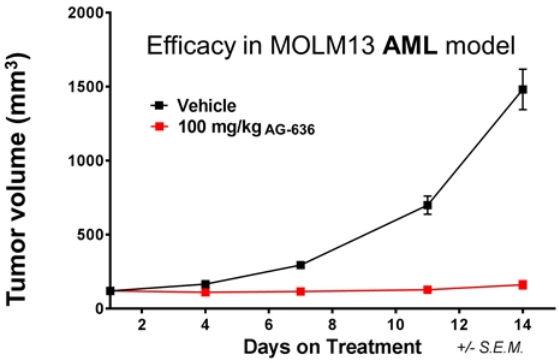


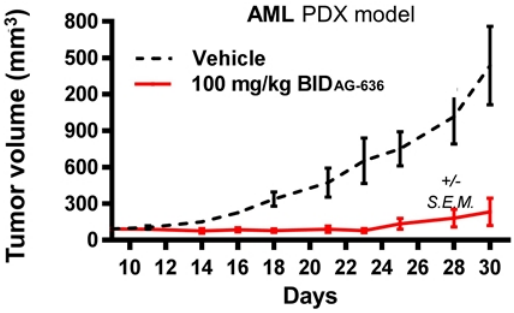
Source: Sykes et al, Cell 2016





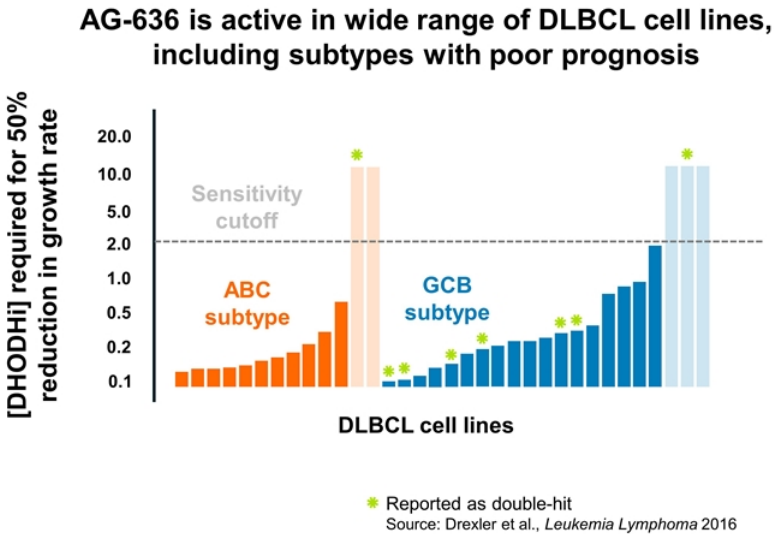
…and drives substantial efficacy *in vivo*

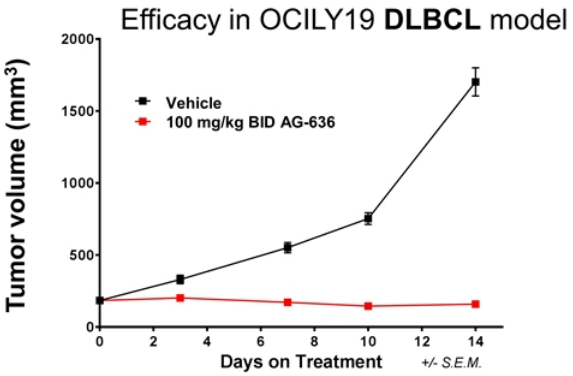


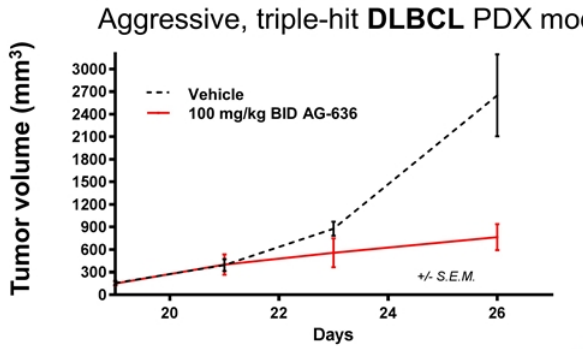


Source: Agios data on file

DHODH Inhibitor AG-636 is Efficacious in DLBCL







Source: Agios data on file

Agios Preclinical Oncology Pipeline

Program	Target Discovery	Target Validation	Drug Discovery	Drug Candidate
Oncology				
Heme Lineage: AG-636 DHODH				●
MAT2A Follow-Ons			●	
Genetically Defined Heme Target			●	
Genetically Defined Solid Tumor Target			●	
Genetically Defined Heme Target		●		
Other Exploratory Programs	◐	◐		

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

Agios Preclinical Pipeline

Program	Target Discovery	Target Validation	Drug Discovery	Drug Candidate
Oncology				
Heme Lineage: AG-636 DHODH				●
MAT2A Follow-Ons			●	
Genetically Defined Heme Target			●	
Genetically Defined Solid Tumor 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

Q&A

Ivosidenib Clinical Strategy in Acute Myeloid Leukemia

Darrin Miles, Vice President, IDH Program Management

IDH Mutations Across Many Tumor Types

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

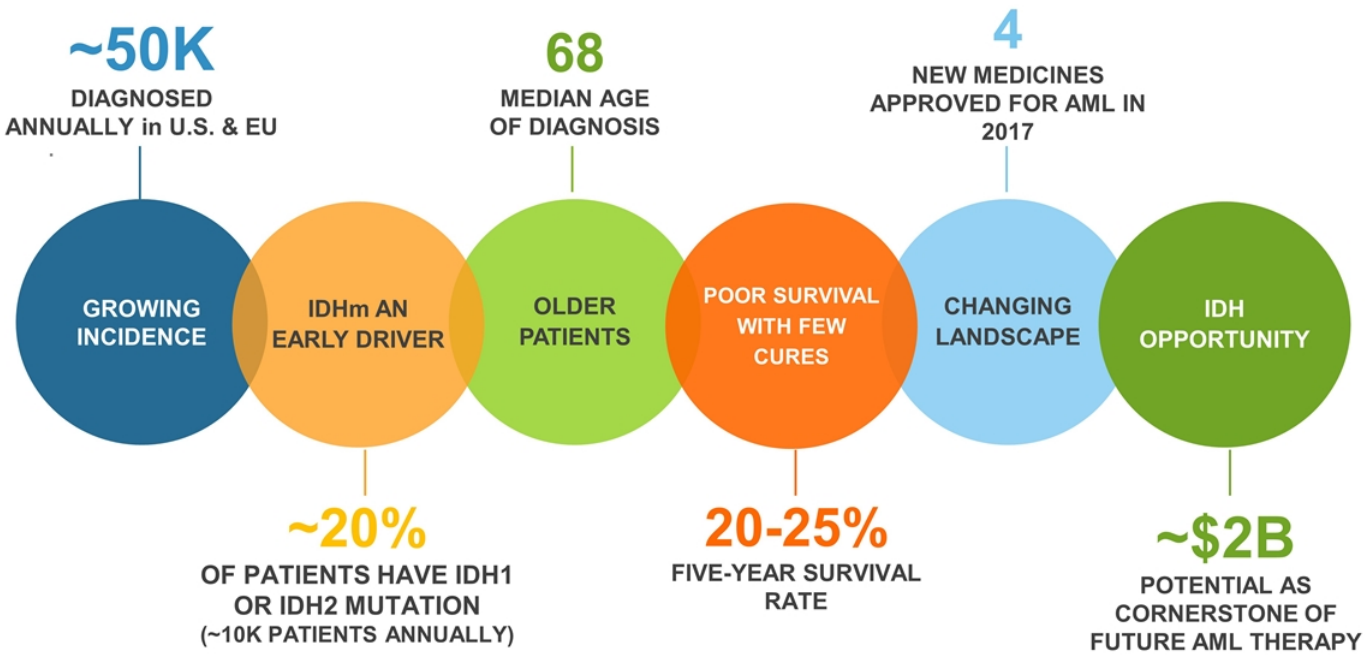
MYELODYSPLASTIC SYNDROMES

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

CHONDROSARCOMAS

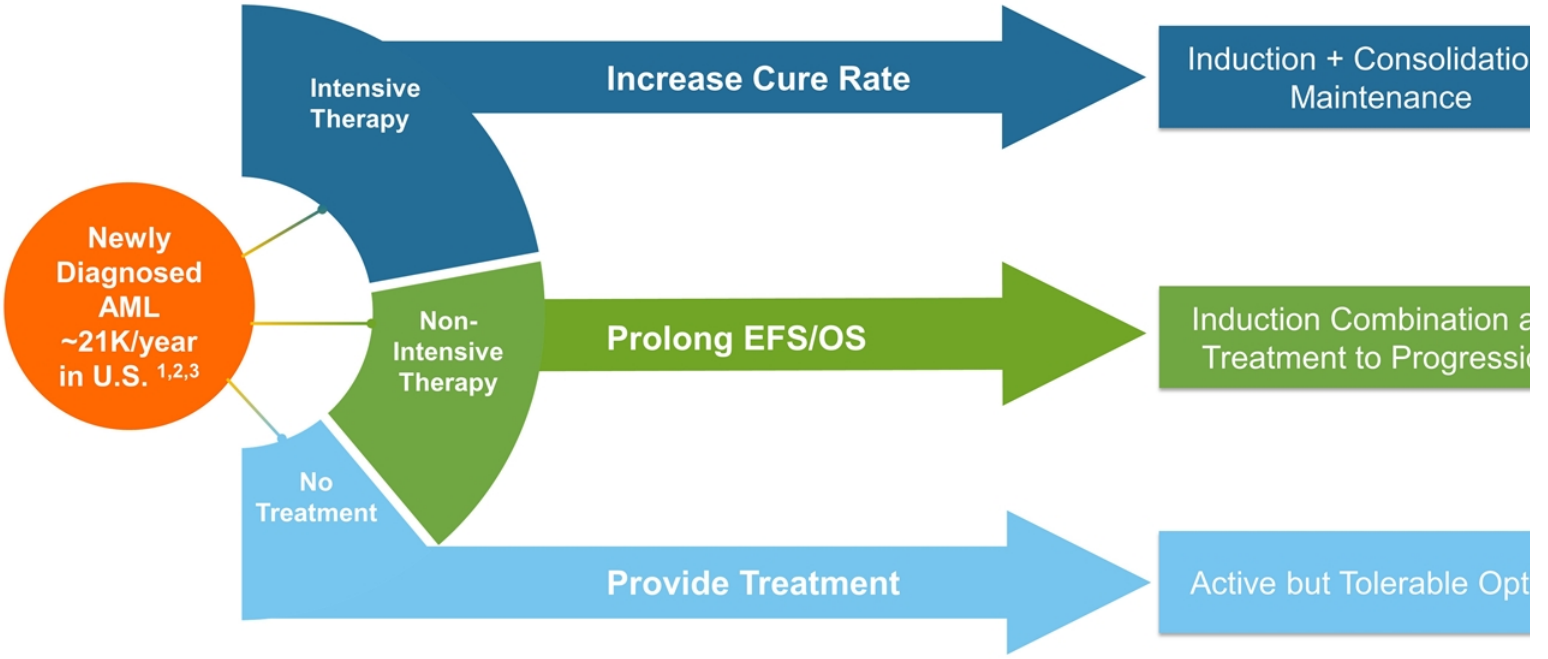
- *IDH1m R/R Ivosidenib Phase 1 Enrollment Complete*

AML Landscape on the Brink of a Therapeutic Tidal Shift



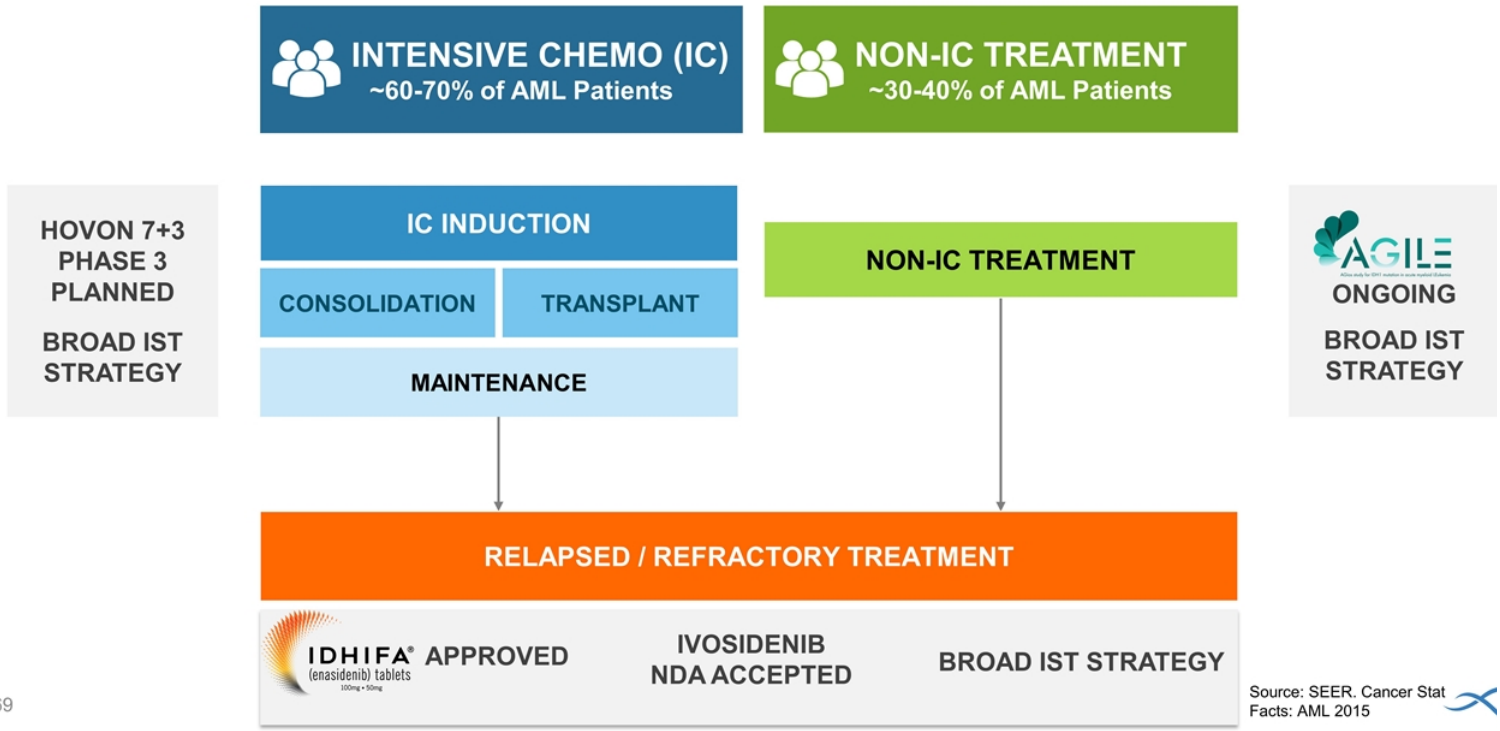
Sources: SEER. Cancer Stat Facts: AML 2015 and Epiphany EPIC oncology numbers; American Cancer Society. AML 2017.; Visser et. Al. Incidence, survival and prevalence of myeloid malignancies in Europe. Eur J Cancer. 2012 Nov;48(17):3257-66; Thomas ED, N Engl J Med. 1979 Mayer, N Engl J Med. 1994, Fernandez 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

Shifting the Treatment Paradigm for AML with Precision Medicine



Sources:1) SEER. Cancer Stat Facts: AML 2015. 2) American Cancer Society. AML 2017. 3) 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

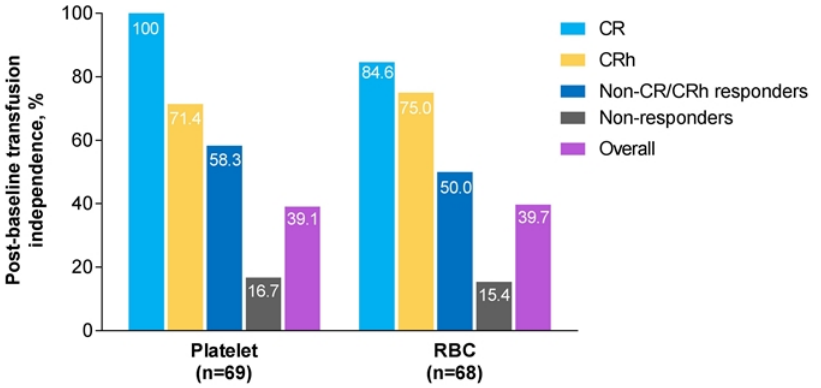
Clinical Development of IDHm Inhibitors Spans All Treatment Lines to Become Cornerstone of Treatment



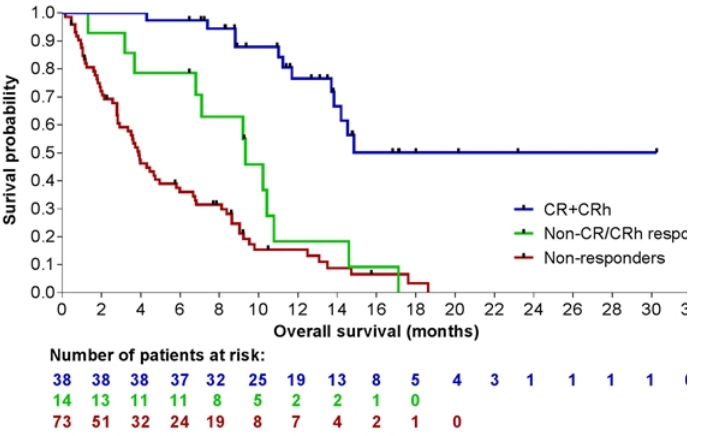
Source: SEER. Cancer Stat Facts: AML 2015

Ivosidenib Phase 1 R/R AML Data

Transfusion Independence Across All Response Categories



Overall Survival by Best Response in R/R AML (n=12



- Median OS 8.8 months overall
  - mOS for CR+CRh has not been reached
  - 9.3 months for non-CR+CRh responders
  - 3.9 months for non-responders
- Median follow-up, 14.8 months

Source: Data from ASH 2017
Data cutoff: 12May2017. CR, complete remission; CRh, CR with partial hematologic recovery; RBC, red blood cell

30.4% CR+CRh rate w/ median duration of 8.2 months (125 patient primary analysis set); Data to be updated at ASCO

Ivosidenib Phase 1 – Response in Untreated AML and MDS

Characteristics
Untreated AML = patients not eligible for standard of care
Median age (years) • Untreated AML – 76.5 • MDS – 72.5

Response Rates	Untreated AML Arm 2[a] (n=34)	MDS Arm 3[b] (n=12)
Overall Response Rate, n (%) [95% CI]	**19 (55.9) [37.9, 72.8]**	**11 (91.7) [61.5, 99.8]**
Duration of response, median [95% CI] months	9.2 [1.9, NE]	NE [2.3, NE]
Duration of CR, median [95% CI] months	NE [5.6, NE]	NE [2.8, NE]
Best response, n (%)		
CR	7 (20.6)	5 (41.7)
CRi/CRp	7 (20.6)	n/a
PR	1 (2.9)	n/a
MLFS/mCR	4 (11.8)	6 (50.0)
SD	10 (29.4)	0
PD	3 (8.8)	1 (8.3)
NA	2 (5.9)	0

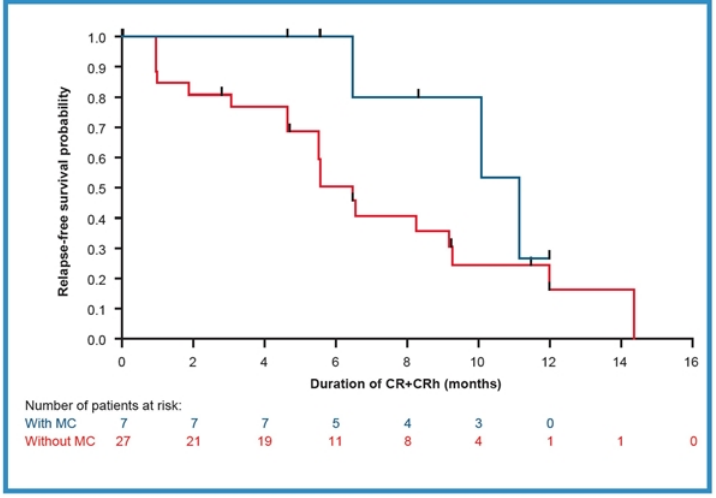
Source: Data from ASH 2017

[a]Untreated AML patients not eligible for standard of care therapies in expansion Arm 2 and from dose escalation whose starting dose was 500 mg QD

[b]MDS patients in expansion Arm 3 and from dose escalation whose starting dose was 500 mg QD

Molecular MRD-Negative CR Associated with Prolonged Duration of CR+CRh and Improved Overall Survival (R/R AML, BMMCs)

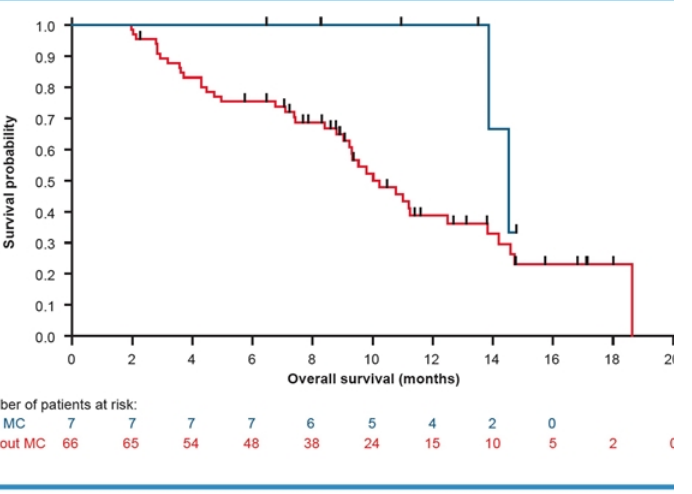
Duration



Number of patients at risk:

With MC	7	7	7	5	4	3	0		
Without MC	27	21	19	11	8	4	1	1	0

Overall Survival



Number of patients at risk:

With MC	7	7	7	7	6	5	4	2	0	
Without MC	66	65	54	48	38	24	15	10	5	2

MC = Mutation Clearance, defined as the inability to detect the *mIDH1* variant allele (lower limit of detection for *mIDH1* alleles of 0.02–0.04% ($2–4\times10^{-4}$) from ≥1 on-study time point in a patient with detectable *mIDH1* at screening.
Duration of CR+CRh = date of first documented CR/CRh to date of first documented confirmed relapse or death
Overall survival = time from first dose to the date of death due to any cause
BMMC = bone marrow mononuclear cells
Statistical testing not provided owing to small sample size and low event rate

— With MC — Without MC | Censored

Source: Data from ASH 2017

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 expected at ASH

Ivosidenib plus Azacitidine n=11

- Median age 76 years
- Combination safe & well tolerated
- ORR rate = 8 of 11
- CR rate = 4 of 11

Updated data at ASCO

Source: Data from ASH 2017

Opportunity to Utilize Event-Free Survival (EFS) as Primary Endpoint

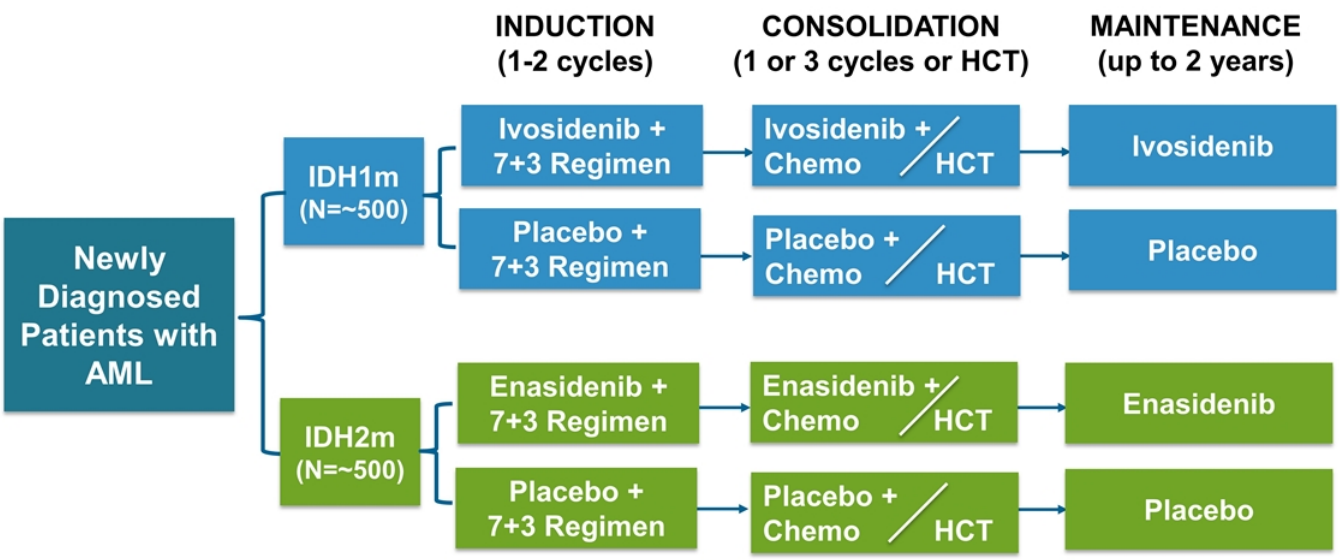
"Improvement in EFS itself represents benefit to patients"
FDA ASH 2017

- Recent FDA/EMA approval of treatment for newly diagnosed de novo AML based on EFS primary

Evaluating change of Phase 3 AGILE primary endpoint to EFS

- Like OS, an EFS endpoint will reflect direct clinical benefit of ivosidenib but can be achieved faster than OS
- EFS endpoint enables patient cross-over and is not impacted by subsequent treatments

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



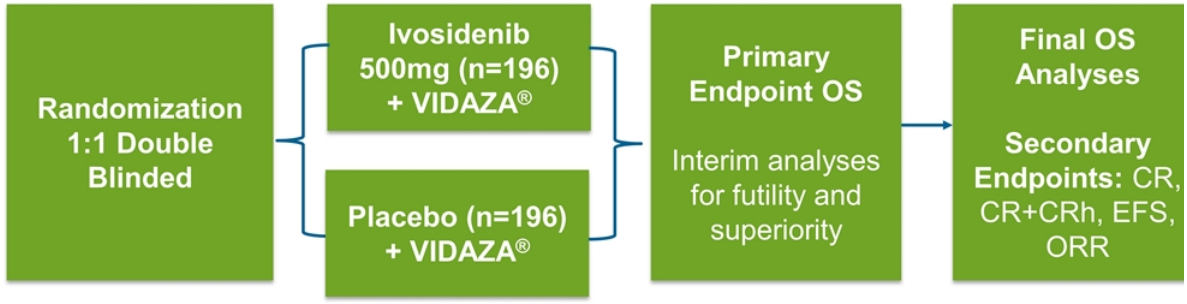
EFS = Event Free Survival
HCT = Hematopoietic Cell Transplantation

EFS primary endpoint; sponsored by HOVON and AML-SG

Phase 3 Frontline AGILE Ongoing

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

Executing a Broad IST Strategy

Trial Design	Line
Ongoing	
Venetoclax combination	R/R AML; potential frontline*
Beat AML master trial (+ VIDAZA®)**	Frontline AML
Planned	
Maintenance**	Frontline AML post stem cell transplant
VYXEOS™ combination	R/R AML
VYXEOS™ combination	Secondary AML
Gilteritinib combination**	R/R AML; potential frontline
MDS monotherapy**	Frontline and R/R AML
MEKi combination	R/R AML; potential frontline
ATRA combination	R/R AML; potential frontline

* potential to enroll patients who opt out of standard of care treatment or are otherwise considered ineligible
** Study includes ivosidenib and IDHIFA ®
VIDAZA® is a registered trademark of Celgene Corporation
VYXEOS™ is a trademark of Jazz Pharmaceuticals

Accepted ASCO Abstracts

Updated data from expansion phase of the Phase 1 study of ivosidenib in IDH1m R/R AML accepted to ASCO

Updated data from the Phase 1/2 combo trial of enasidenib or ivosidenib with VIDAZA® in newly diagnosed AML accepted to ASCO

First clinical data from the Phase 1 study of AG-881 in advanced IDHm positive solid tumors, including glioma, accepted to ASCO

Ivosidenib Commercial Strategy in Acute Myeloid Leukemia

Steve Hoerter, Chief Commercial Officer

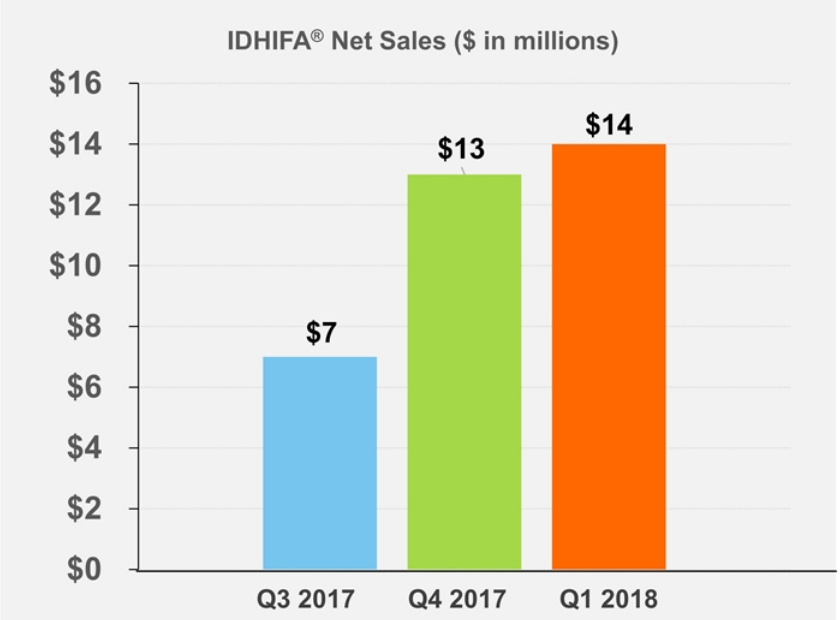
Building the Agios IDH Commercial Franchise

IDHIFA® commercial performance update

Scoping the IDH1 AML opportunity

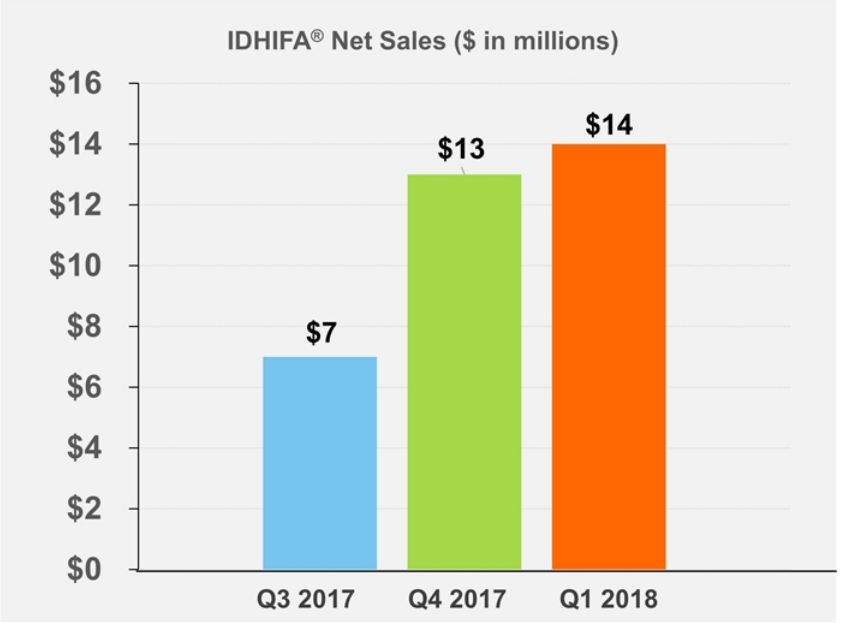
Ivosidenib launch preparations

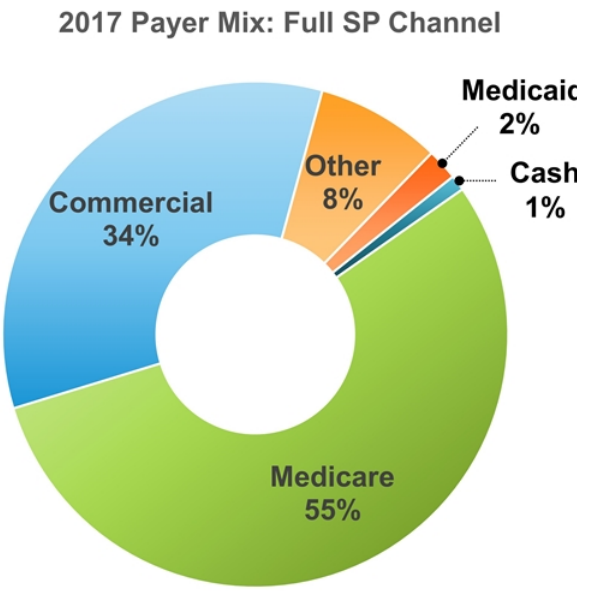
IDHIFA® Launch Performance



Revenues reported by Celgene; 2017 Payer Mix, Agios Estimates

IDHIFA® Launch Performance





Revenues reported by Celgene; 2017 Payer Mix, Agios Estimates

IDHIFA® Launch Metrics Are on Track

Sales	Diagnostic Testing	Prescriber Base	Awareness
Early IDHIFA® Success			
2017 sales **$20M (Q4 sales $13M)**	IDH2m testing at **~50% as of October**	**>250** unique prescribers	IDHIFA® awareness of **~50% as of October**
IDHIFA® Launch Metrics Update			
2018 Q1 sales **$14M**	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

NCCN Treatment Guidelines Address IDHm+ AML

Molecular Testing

IDH1 and IDH2 molecular analyses recommended for workup of all AML cases

IDH2 Mutated AML

Enasidenib is recommended in patients with relapsed/refractory AML and an IDH2 mutation

Enasidenib added as an option in the first-line setting in patients who are not candidates for intensive remission induction therapy, or who decline intensive therapy

For patients who respond to first-line therapy with enasidenib, recommendation is to continue until disease progression

- Footnote added: Response to treatment with enasidenib may take 3-5 months
- Footnote added: Enasidenib increases the risk for differentiation syndrome and hyperleukocytosis that may require treatment with hydroxyurea and steroids

Source: NCCN version I.2018, updated February 7, 2018

Promotional efforts are limited to the IDH2m+ relapsed/refractory AML population

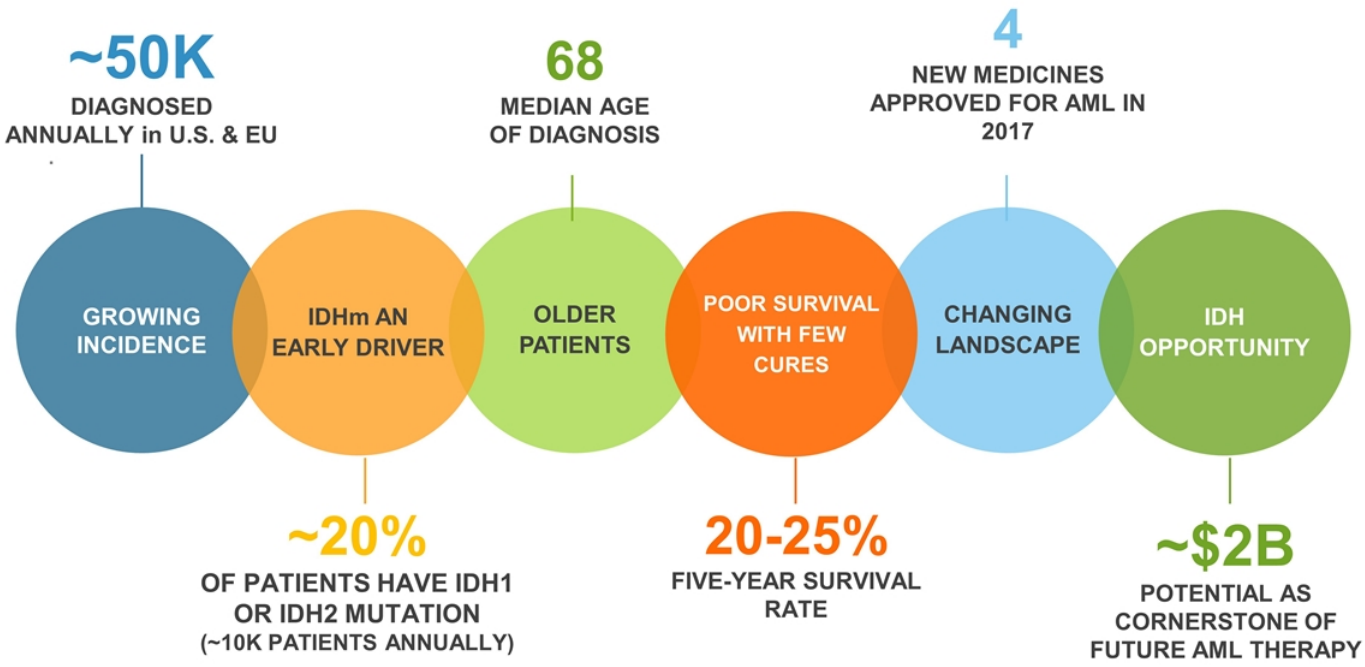
Building the Agios IDH Commercial Franchise

IDHIFA® commercial performance update

Scoping the IDH1 AML opportunity

Ivosidenib launch preparations

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

New Medicines to Treat AML: Great News for Patients

Pre-2017

Fit for Intensive Chemotherapy

Not Fit for Intensive Chemotherapy

Treatments based on patients eligibility (or not) for intensive chemotherapy

Today & The Future

RYDAPT® midostaurin 25 mg capsules

IDHIFA® (enasidenib) tablets 100mg • 50mg

Targeted treatments offering personalized approach

MYLOTARG™ gemtuzumab ozogamicin INJECTION FOR IV INFUSION 4.5 mg single-dose vial

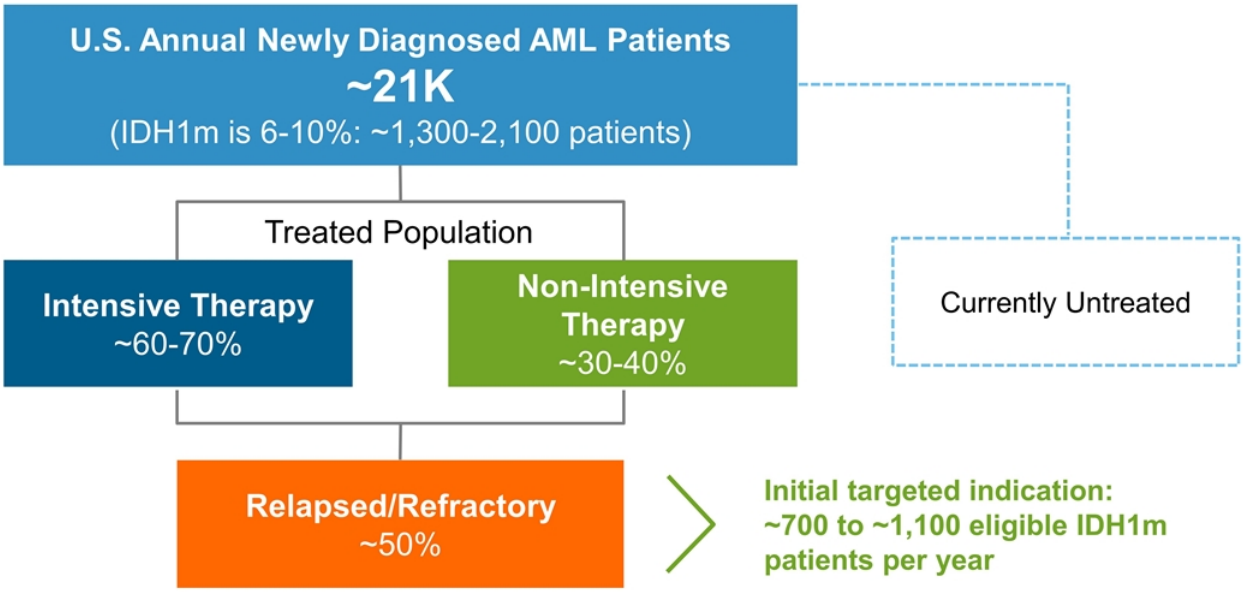
Vyxeos™ daunorubicin and cytarabine liposome for injection

Unselected treatments that offer improvements over current SoC

How We Taught Ourselves to Pronounce Ivosidenib

How We Taught Ourselves to Pronounce Ivosidenib

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.

Building the Agios IDH Commercial Franchise

IDHIFA® commercial performance update

Scoping the IDH1 AML opportunity

Ivosidenib launch preparations

Strategic Imperatives for the TIBSOVO® Launch

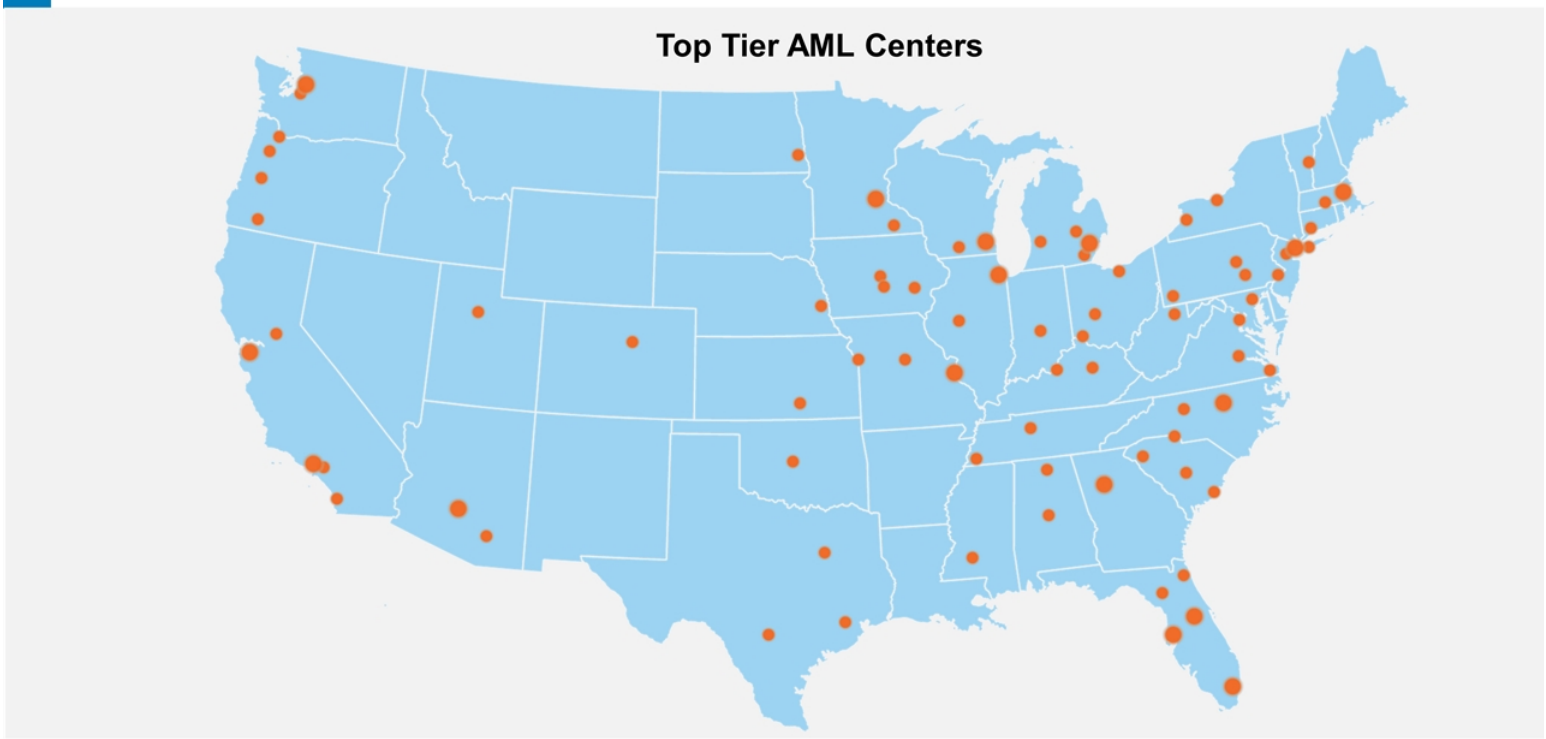
Physicians test for IDH1m

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

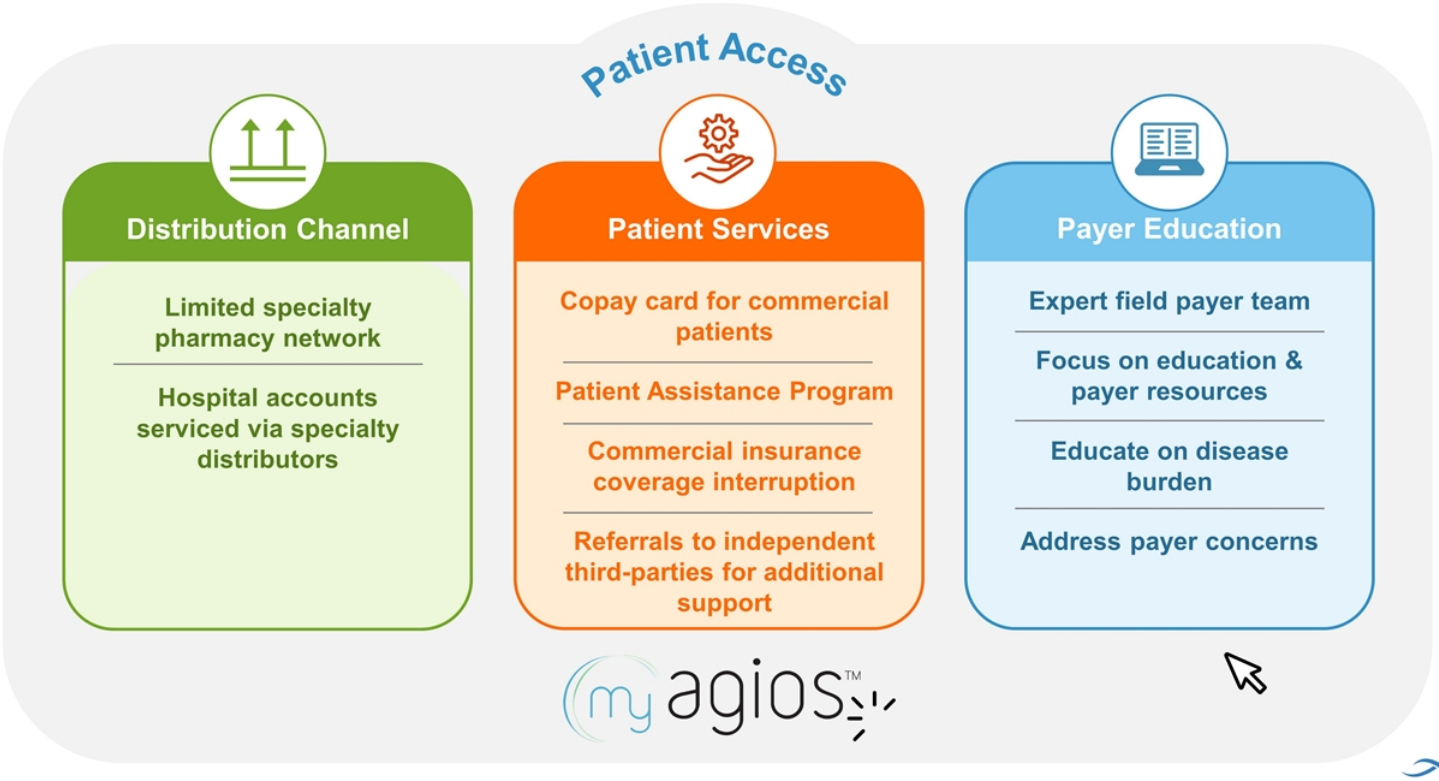
TIBSOVO® (ivosidenib) tablets

Patients have access to TIBSOVO®

Sales Team Deployed to Cover Prescriber Base



Our Approach to Patient Access is Multifaceted



Welcome to myAgios™

Patient Support Services

Financial assistance programs

Network of specialty pharmacy and distribution partners

Enroll now

We are Launch Ready, Thanks to a Great Team

IDH1m Inhibition in Solid Tumors

Susan Pandya, M.D., Senior Medical Director

IDH1 Mutation Present in Multiple Solid Tumors

CHOLANGIOCARCINOMA
~14% have IDH1 mutation
~3,000 IDH1m patients

- **IDH1m R/R**
  Ivosidenib Phase 3
  (ClarIDHY) Ongoing
- **IDH1m R/R**
  Ivosidenib Phase 1
  Enrollment Complete

LOW GRADE GLIOMA
~80% have IDH1 mutation
~9,000 IDH1m patients

- **IDH1m**
  Ivosidenib & AG-881 Perioperative Study
  Ongoing
- **IDH1m**
  Ivosidenib
  Phase 1 Enrollment Complete
- **IDH1m**
  AG-881
  Phase 1 Enrollment Complete
- **IDH1m**
  Natural History of Tumor Volume

CHONDROSARCOMAS
~50% have IDH1 mutation
~900 IDH1m patients

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

Sources: 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

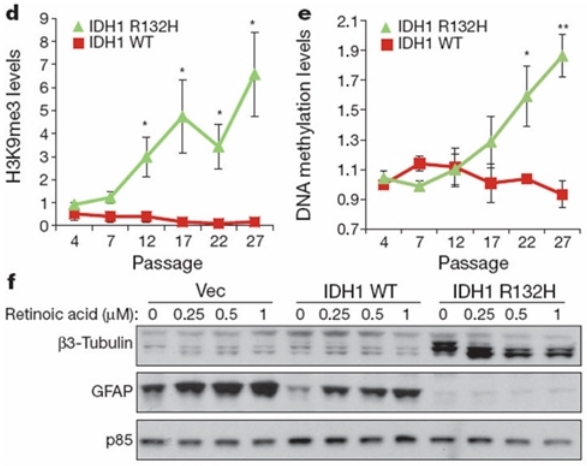
The Story of IDHm Inhibition in Solid Tumors is Evolving

2012

Published in final edited form as:
Nature. ; 483(7390): 474–478. doi:10.1038/nature10860.

IDH mutation impairs histone demethylation and results in a block to cell differentiation

Chao Lu[1,2], Patrick S. Ward[1,2], Gurpreet S. Kapoor[3], Dan Rohle[4,5], Sevin Turcan[4], Omar Abdel-Wahab[4,6], Christopher R. Edwards[7], Raya Khanin[8], Maria E. Figueroa[9], Ari Melnick[9], Kathryn E. Wellen[2], Donald M. O'Rourke[3,10], Shelley L. Berger[7], Timothy A. Chan[4], Ross L. Levine[4,6], Ingo K. Mellinghoff[4,5,11], and Craig B. Thompson[1]



Nature. ; 483(7390): 474–478. doi:10.1038/nature10860

The Story of IDHm Inhibition in Solid Tumors is Evolving

2012 **2013 - 2014**

Science

An Inhibitor of Mutant IDH1 Delays Growth and Promotes Differentiation of Glioma Cells

Dan Rohle, Janeta Popovici-Muller, Nicolaos Palaskas, Sevin Turcan, Christian Grommes, Carl Campos, Jennifer Tsoi, Owen Clark, Barbara Oldrini, Evangelia Komisopoulou, Kaiko Kunii, Alicia Pedraza, Stefanie Schalm, Lee Silverman, Alexandra Miller, Fang Wang, Hua Yang, Yue Chen, Andrew Kernytsky, Marc K. Rosenblum, Wei Liu, Scott A. Biller, Shinsan M. Su, Cameron W. Brennan, Timothy A. Chan, Thomas G. Graeber, Katharine E. Yen and Ingo K. Mellinghoff

Science **340** (6132), 626-630.
DOI: 10.1126/science.1236062originally published online April 4, 2013

LETTER

doi:10.1038/nature134

Mutant IDH inhibits HNF-4α to block hepatocyte differentiation and promote biliary cancer

Supriya K. Saha[1]*, Christine A. Parachoniak[1]*, Krishna S. Ghanta[1], Julien Fitamant[1], Kenneth N. Ross[1], Mortada S. Najem[1], Sushma Gurumurthy[1], Esra A. Akbay[2], Daniela Sia[3,4,5], Helena Cornella[3], Oriana Miltiadous[4], Chad Walesky[6], Vikram Deshpande Andrew X. Zhu[1], Aram F. Hezel[7], Katharine E. Yen[8], Kimberly S. Straley[8], Jeremy Travins[8], Janeta Popovici-Muller[8], Camelia Gliser[8], Cristina R. Ferrone[1], Udayan Apte[6], Josep M. Llovet[3,4,9,10], Kwok-Kin Wong[2], Sridhar Ramaswamy[1,11] & Nabeel Bardeesy[1]

Nature. ; 483(7390): 474–478. doi:10.1038/nature10860

The Story of IDHm Inhibition in Solid Tumors is Evolving

2012 2013 - 2014 **2014 - Present**

AUTHOR'S VIEW

OncoImmunology 3:12, e974392; December 2014; © 2014 Taylor & Francis Group, LLC

Mutant IDH1: An immunotherapeutic target in tumors

Theresa Schumacher[1,2], Lukas Bunse[1,2], Wolfgang Wick[1,3], and Michael Platten[1,2,*]

Neuro-Oncology

Neuro-Oncology 18(10), 1402–1412, 2016
doi:10.1093/neuonc/now061
Advance Access date 25 April 2016

IDH mutant gliomas escape natural killer cell immune surveillance by downregulation of NKG2D ligand expression

Xiaoran Zhang†, Aparana Rao†, Paola Sette, Christopher Deibert, Alexander Pomerantz, Wi Jin Kim, Gary Kohanbash, Yigang Chang, Yongseok Park, Johnathan Engh, Jaehyuk Choi, Timothy Chan, Hideho Okada, Michael Lotze, Paola Grandi, and Nduka Amankulor

CSH PRESS Genes & Development

Mutant IDH1 regulates the tumor-associated immune system in gliomas

Nduka M. Amankulor[1], Youngmi Kim[2], Sonali Arora[2], Julia Kargl[2,3,4], Frank Szulzewsky[2], Mark Hanke[2,3], Daciana H. Margineantu[2,3], Aparna Rao[1], Hamid Bolouri[2,5], Jeff Delrow[6], David Hockenbery[2,3], A. McGarry Houghton[2,3,7] and Eric C. Holland[2,5]

frontiers in Molecular Neuroscience

ORIGINAL RESEARCH
published: 28 March 2018
doi: 10.3389/fnmol.2018.00082

The IDH1 Mutation-Induced Oncometabolite, 2-Hydroxyglutarate, May Affect DNA Methylation and Expression of PD-L1 in Gliomas

Luyan Mu[1,2], Yu Long[1,3], Changlin Yang[3], Linchun Jin[1,3], Haipeng Tao[1,3], Haitao Ge[1], Yifan E. Chang[3†], Aida Karachi[3], Paul S. Kubilis[3], Gabriel De Leon[3†], Jiping Qi[4], Elias J. Sayour[3], Duane A. Mitchell[3], Zhiguo Lin[1] and Jianping Huang[3*]*

Nature. ; 483(7390): 474–478. doi:10.1038/nature10860

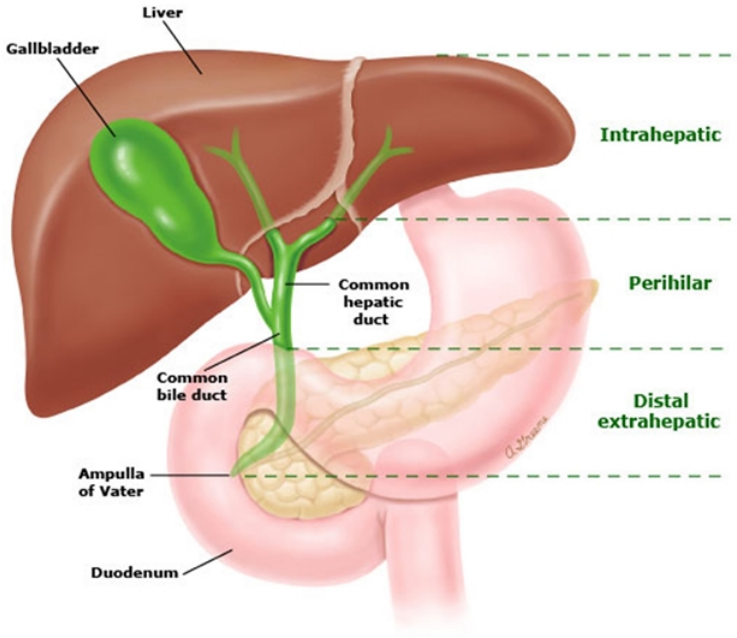
Opportunity for an IDH1m Inhibitor in Solid Tumors

- Frequency of IDH1 mutation in a variety of solid tumors + unmet need in these indications = opportunity to make a difference in the treatment paradigm for these patients
- Active clinical development plans in cholangiocarcinoma & glioma
- Understanding the IDH mutation's role in the treatment of solid tumors is evolving
- Opportunity for IO combinations

Cholangiocarcinoma

Maeve Lowery, M.B., B.Ch., B.A.O., Trinity College Dublin

Cholangiocarcinoma a Devastating Disease with No Approved Targeted Therapies



Symptoms:

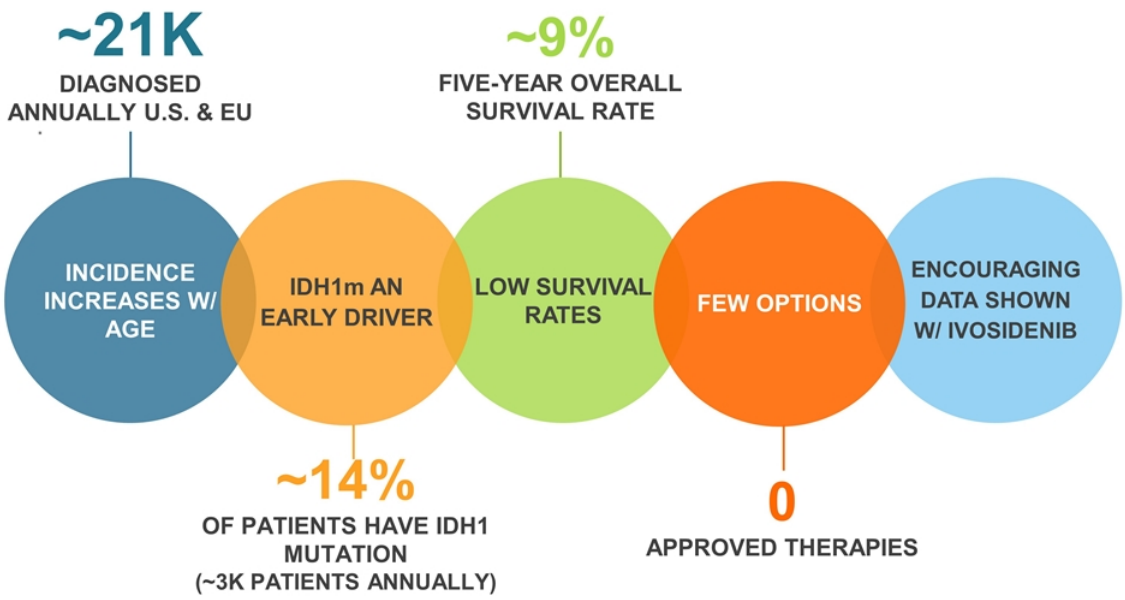
- Abdominal pain (30-50%)
- Weight loss (30-50%)
- Fever (20%)
- Itching
- Jaundice

Increase in laboratory tests:

- Alkalane phosphastase
- GGT
- Total (direct) bilirubin
- AST/ALT
- CA 19-9 (elevated in ~65% cholangiocarcinoma)

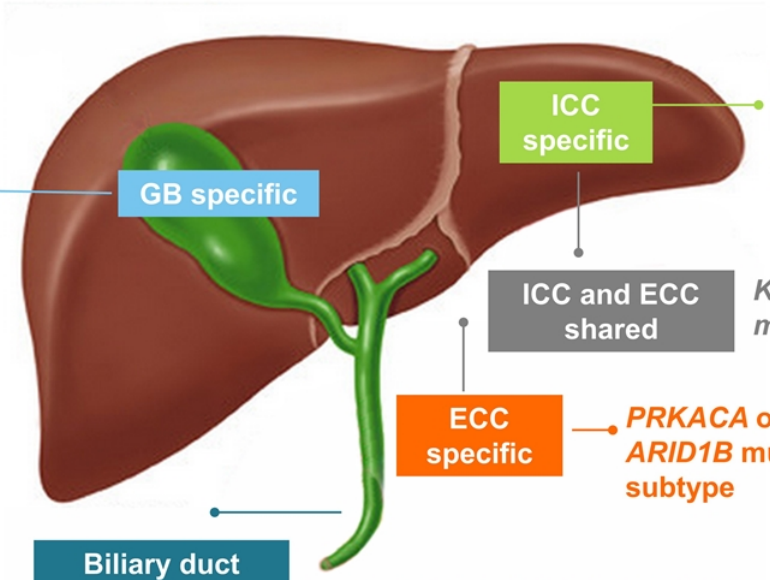
 Sources: http://www.alltohealth.com; www.uptodate.com; https://gi.jhsps.org

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.

Genetic Alterations in Biliary Tract Cancer



EGFR, ERBB3, PTEN, ARID2, MLL2, MLL3, TERT promoter mutation APOBEC signature

GB specific

ICC specific

FGFR2 fusion IDH1/2, EPHA2, BAP1 mutation

C>T at CpG signature

ICC and ECC shared

KRAS, SMAD4, ARID1A, GNAS mutation

ECC specific

PRKACA or *PRKACB* fusion, *ELF3, ARID1B* mutation, better prognosis subtype

Biliary duct common

TP53, BRCA1, BRCA2, PIK3CA mutation

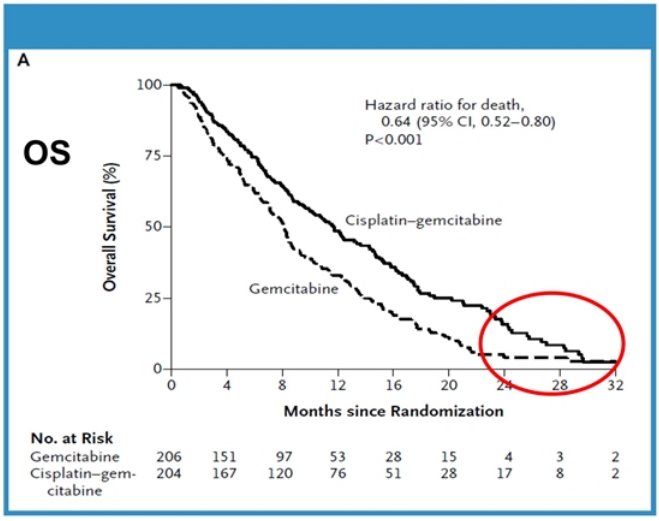
Poor-prognosis subtype with high immune checkpoint activity

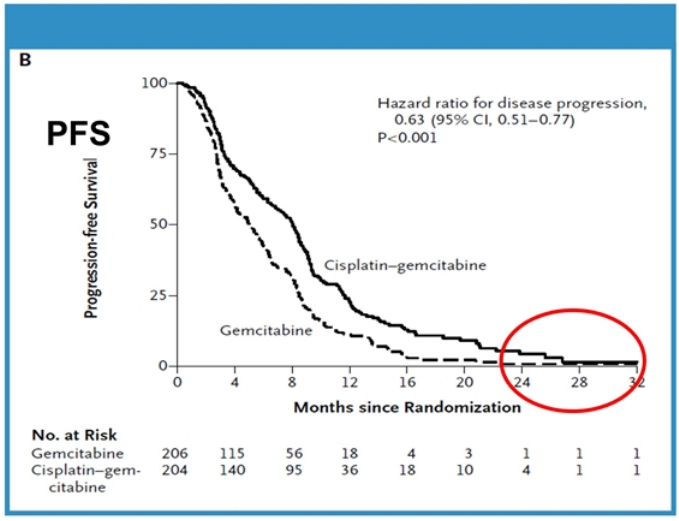
Source: © Nakamura et al, Nature Genetics 2015

Current Treatments are Limited to Chemotherapy-Based Regimens

Phase 3 ABC-02 Gemcitabine and Cisplatin – standard of care for newly diagnosed metastatic disease

- OS – 11.7 months Gem/Cis vs. 8 months for Gem alone
- PFS – 8 months for Gem/Cis vs. 5 months for Gem alone





Source: Valle J. N Engl J Med. 2010

Outcomes with Second Line Chemotherapy Remain Poor and Highlight Need for Novel Treatments

- Median PFS range is 2-3 months and PFS6 is 10-25%
- No available historic placebo PFS benchmark

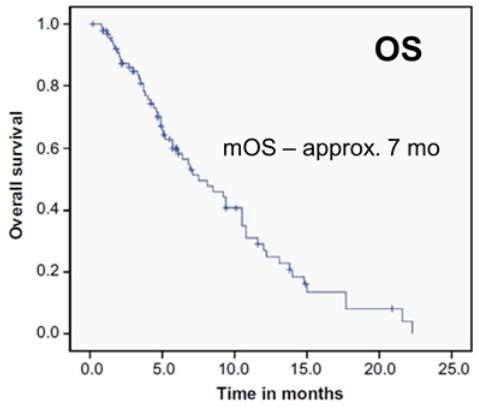


Fig. 2. Overall survival curves from the beginning of second-line chemotherapy in patients with advanced biliary tract cancer.

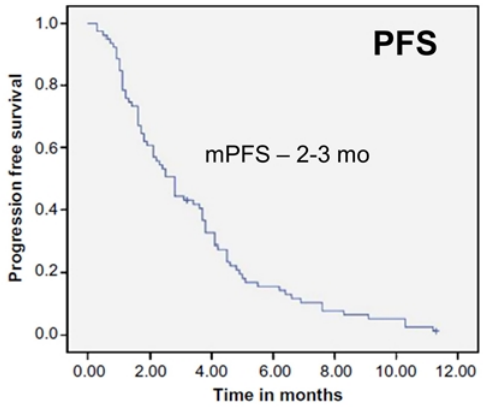
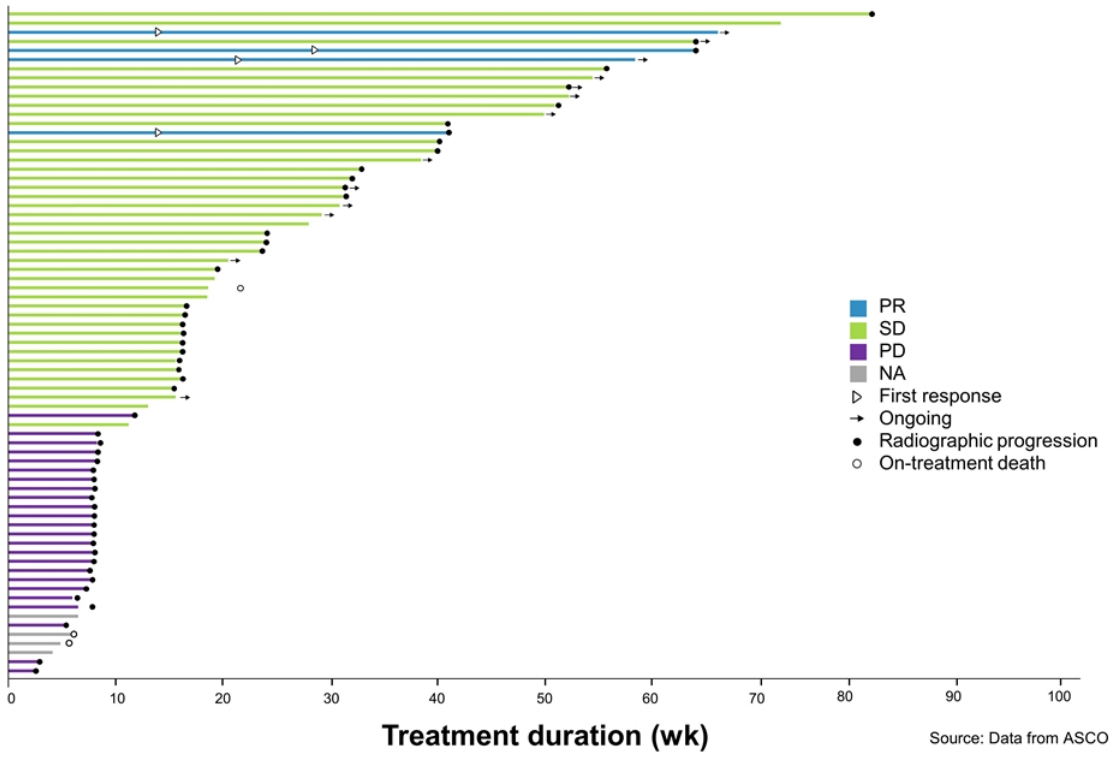


Fig. 1. Progression free survival curve from the beginning of second-line chemotherapy in patients with advanced biliary tract cancer.

Sources: T. Walter et al. / European Journal of Cancer 49 (2013) 329-335

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

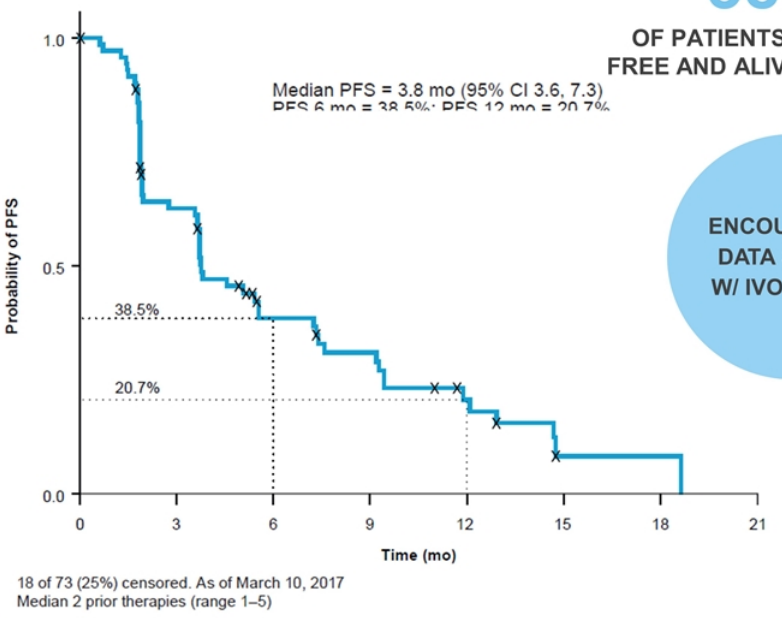
61% disease control rate (PR + SD)



Source: Data from ASCO 2017

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%

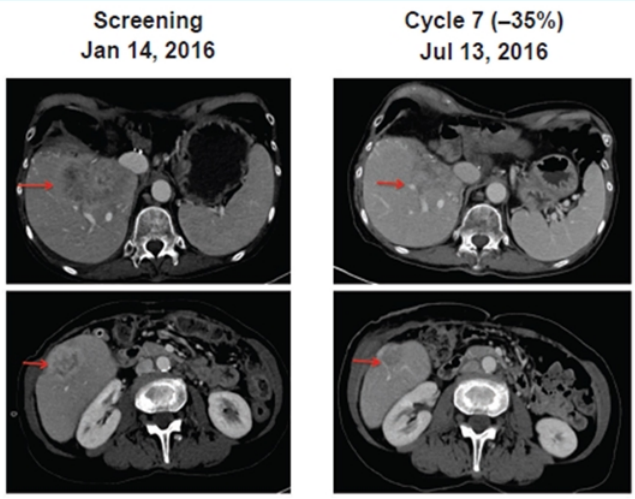
OF PATIENTS PROGRESSION FREE AND ALIVE AT SIX MONTH

ENCOURAGING DATA SHOWN W/ IVOSIDENIB

Source: Data from ASCO 2017

Radiographic Changes in a Patient with a PR on Ivosidenib

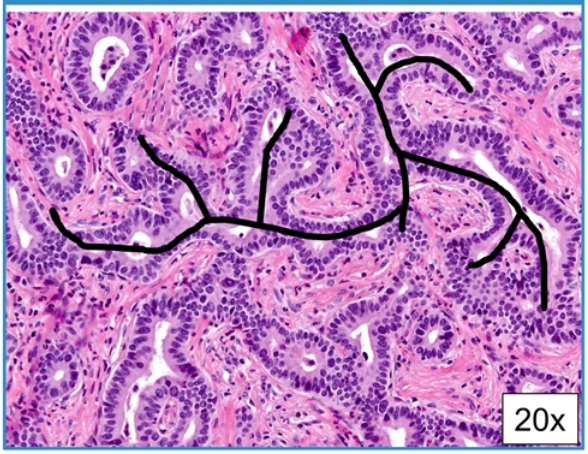
Computed tomography scans of a 66-year-old woman with intrahepatic CC previously treated with neoadjuvant cisplatin + gemcitabine who then received AG-120



Source: Data from ASCO 2017

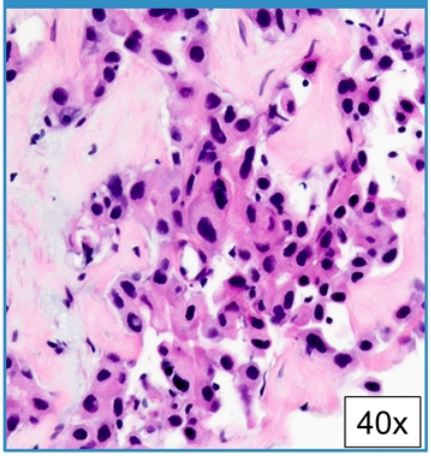
Ivosidenib Promotes Morphologic Changes to Cholangiolar Patterns

Cholangiolar pattern[4]



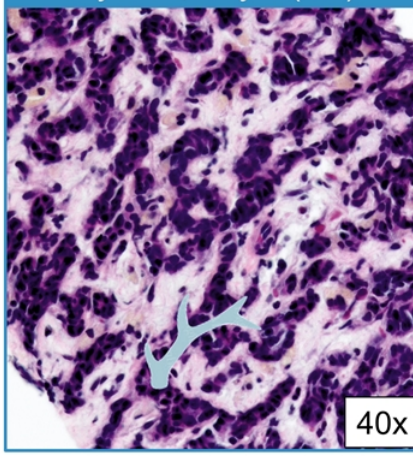
- 'Normal' cholangiolar pattern composed of glands in the shape of antler horns[1-3]
- Associated w/ better clinical outcomes in patients w/ ICC [1,4]

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: NCT0298

Expect to complete enrollment in 1H 2019

Clinical Development in Glioma

Susan Pandya, M.D., Senior Medical Director

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

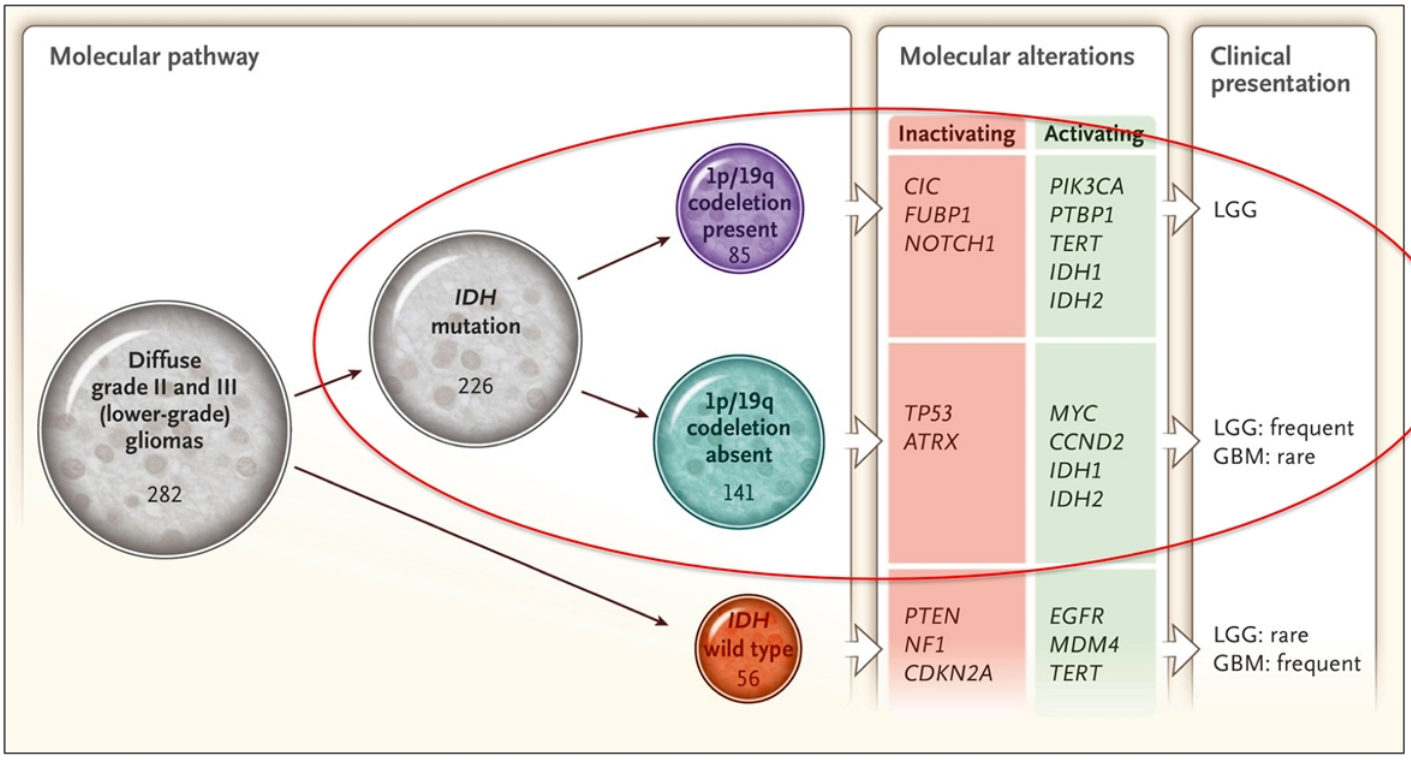
Mean age of diagnosis of 41

~80% of LGG patients present with seizure as initial symptom and up to 90% of patients wil have seizures during disease course

Acute and chronic toxicity associated with chemotherapy and radiation can lead to progressive decline in quality of life (e.g. neurocognitive impairment)

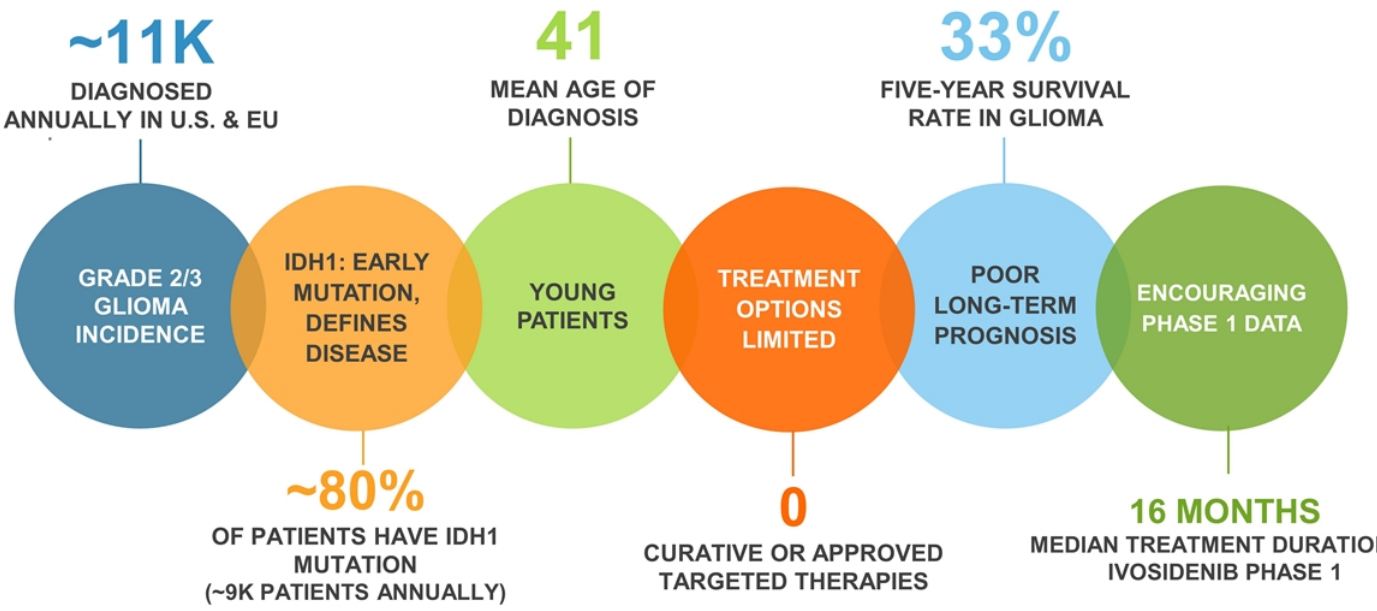
Sources: Semin Radiat Oncol 25:219-224; NATURE REVIEWS | NEUROLOGY, APRIL 2016 | VOLUME 12, 204-2016

IDHm Glioma Is a Distinct Disease



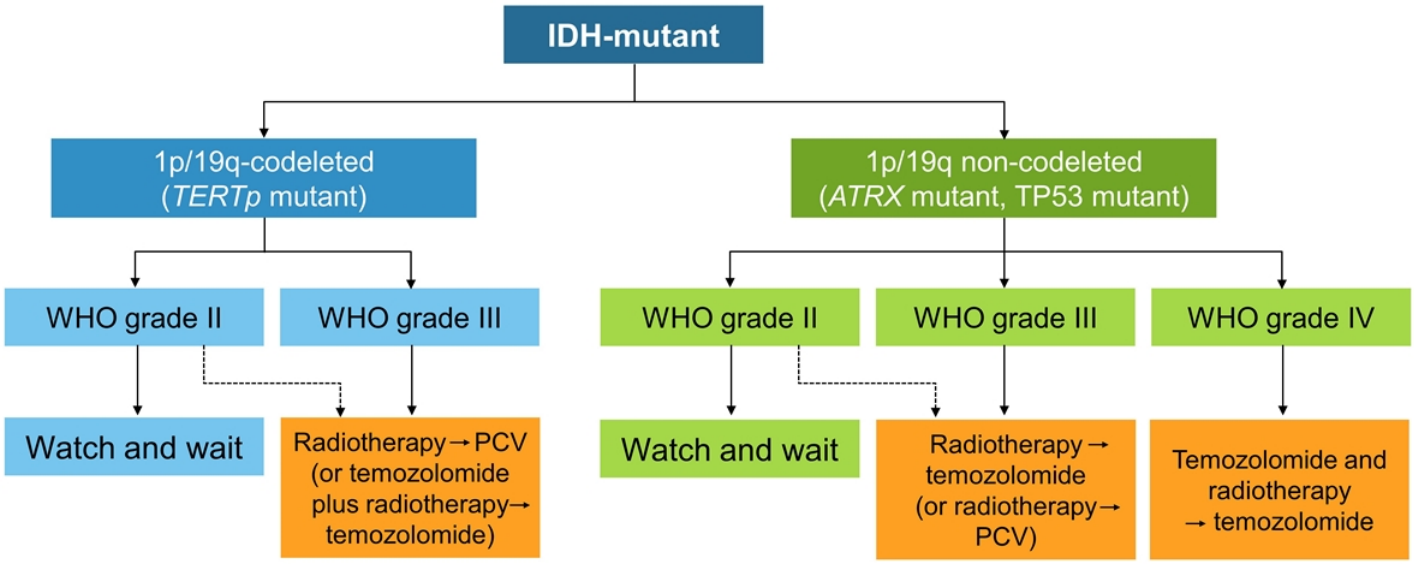
Source: N Engl J Med 2015;372:2481-98

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.

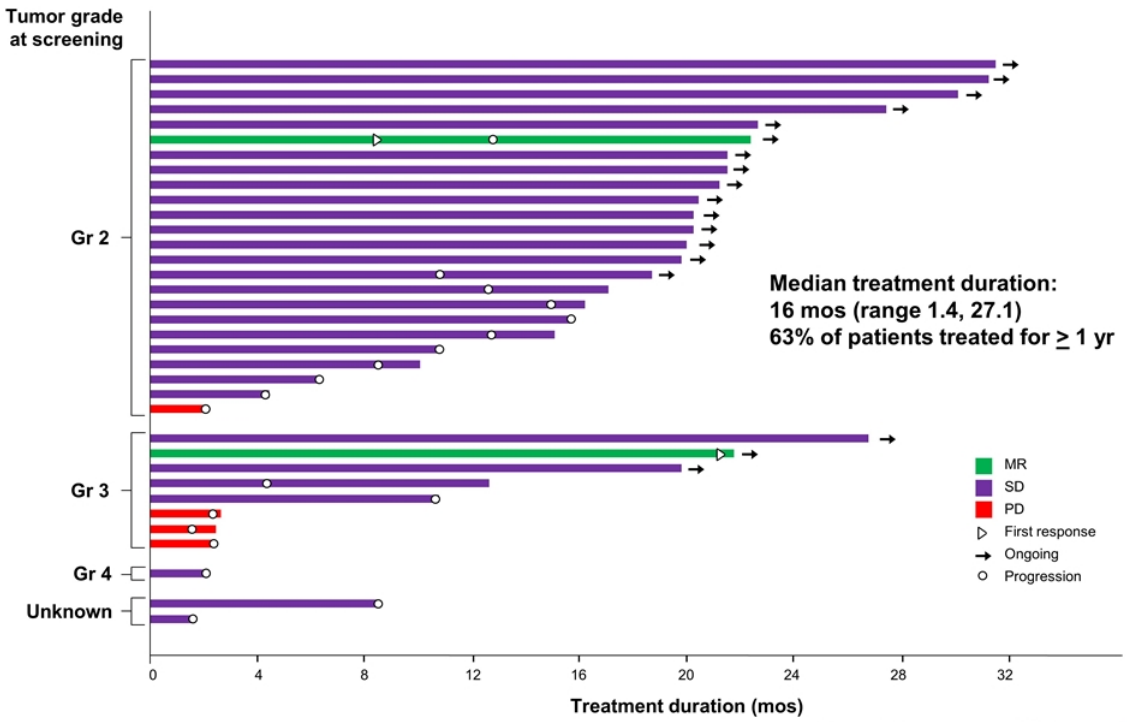
Current Treatment Paradigm for IDHm Gliomas



Source: Lancet Oncol 2017; 18: e315–29

Durable Stable Disease Signal with Ivosidenib Phase 1 Data

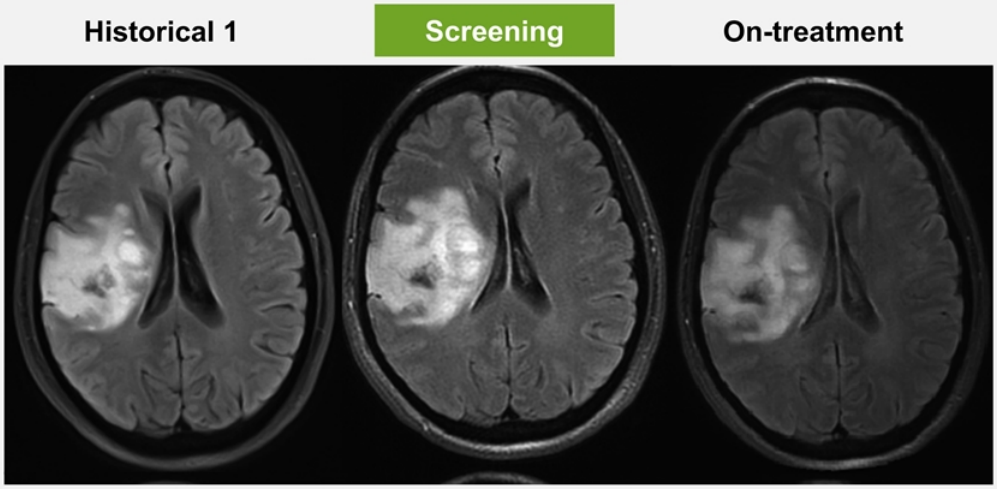
- Ivosidenib well tolerated
- Durable stable disease signal encouraging; 51% of patients still on treatment
- Reduction of tumor growth rates also observed



Source: Data presented at SNO 2017

Ivosidenib Phase 1 Data – Reduction in Tumor Growth Rate

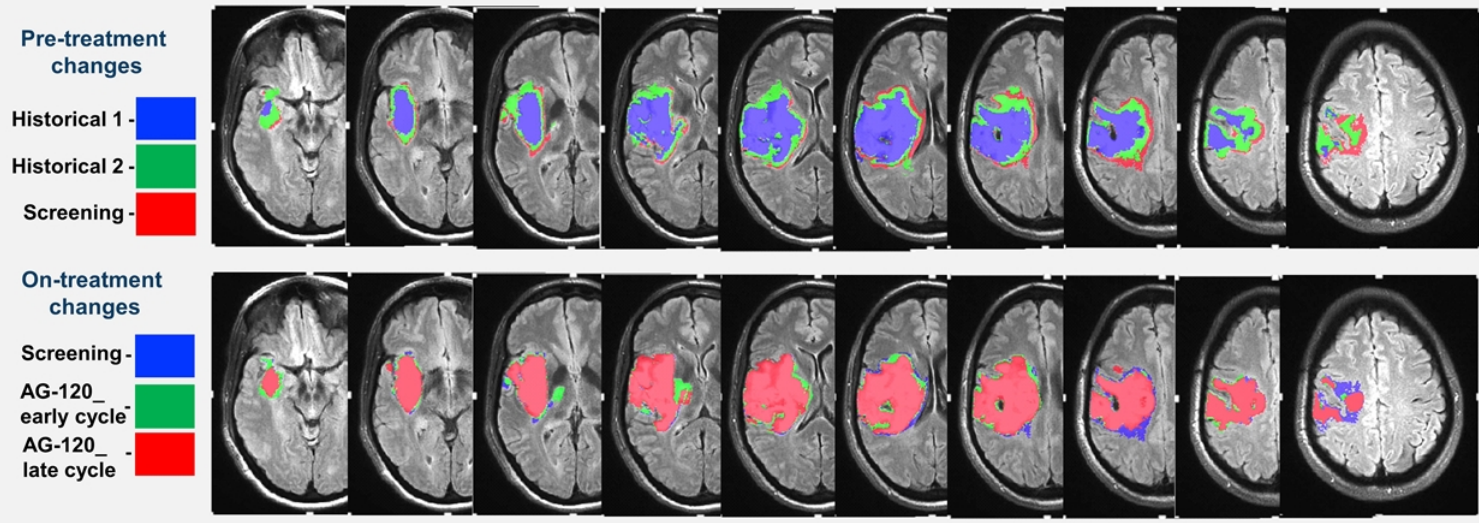
- Oligodendroglioma 1p19q co-del
- Biopsy 2007
- Temozolomide 2007-2008
- No Radiation
- AG-120 Start 10/2015
  H1 MRI: 10/2014
- Remains on treatment (18 mos @ cutoff)
  Best RANO response: SD



H1 = historical pre-treatment scans; Screen = screening

Source: Data presented at SNO 2017

Ivosidenib Phase 1 Data – Reduction in Tumor Growth Rate

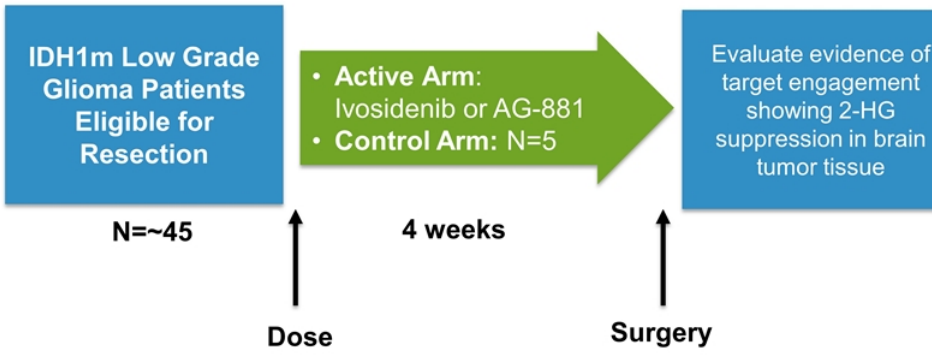


Source: Data presented at SNO 2017

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

Study Objectives:

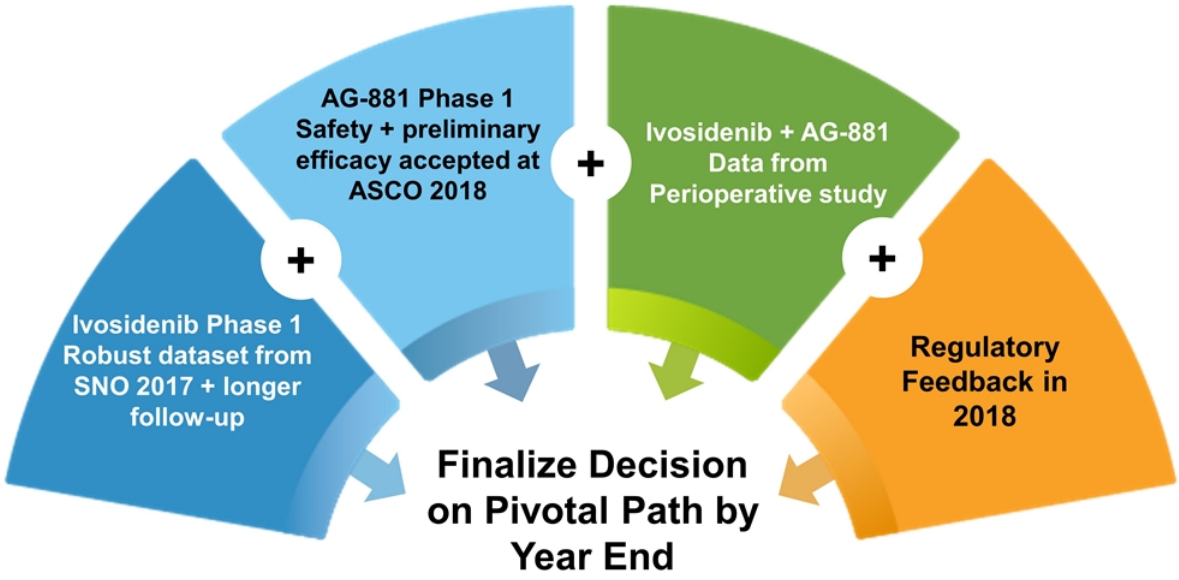
- Determine amount of drug penetration in the brain
- Confirm magnitude of IDHm target engagement as measured by 2HG levels in brain tumor tissue (pre-clincally 85% seen with ivosidenib & 98% with AG-881)
- Assess impact of IDHm inhibition on differentiation and epigenetic profiles in tumor tissue
-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



ClinicalTrials.gov Identifier: NCT033

Trial initiated in Q1; Patients Enrolling

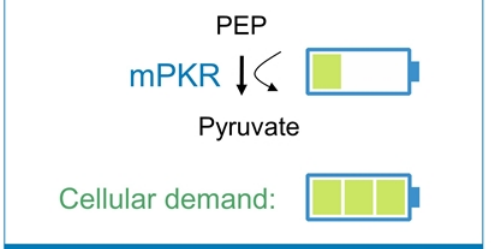
Next Steps in Glioma



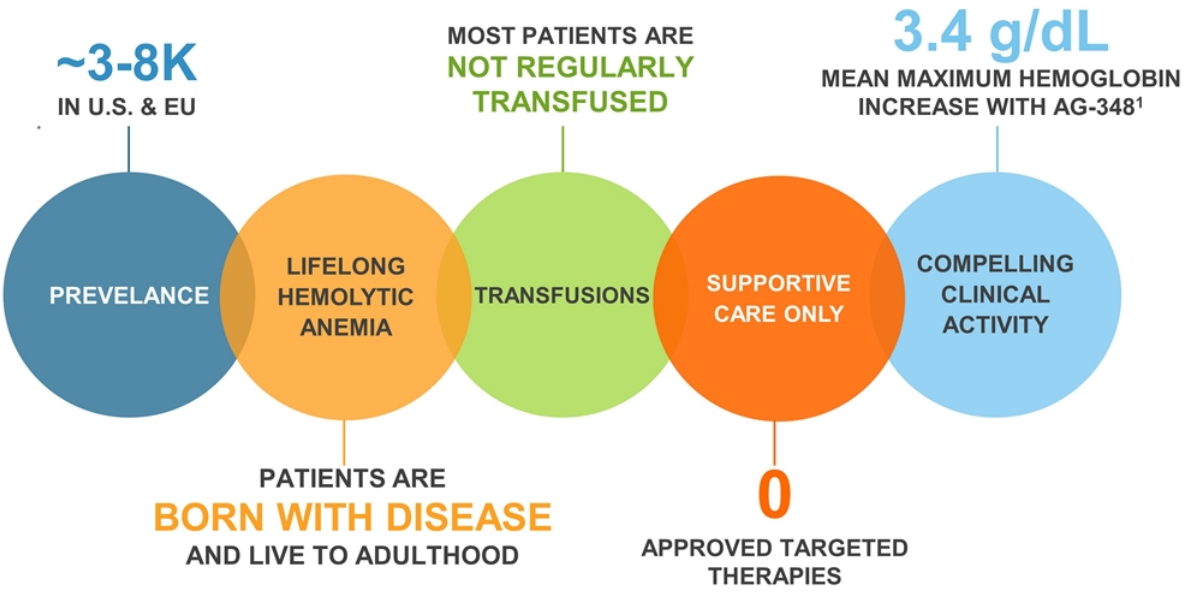
PKR Activation & PK Deficiency

Chris Bowden, M.D., Chief Medical Officer

PK Activation Represents Opportunities Across Hemolytic Anemias

Normal Red Cell	Pyruvate Kinase Deficiency	Other Hemolytic Anemias
		
ATP production meets demand	**Inadequate production: ATP deficiency**	**Increased demand: ATP deficiency**
	✓ **Proof of concept achieved**	**Thalassemia:** Expect to initiate Phase 2 proof-of-concept study in Q4 2018 **Sickle cell:** Planning underway

Opportunity for 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

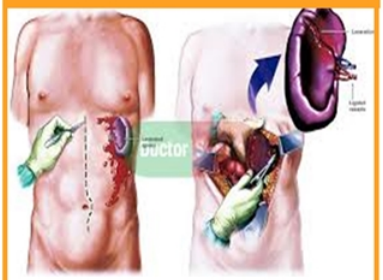
ACTIVATE-T initiated and ACTIVATE to begin in Q2 2018

PK Deficiency Carries Lifelong Burden

Infants

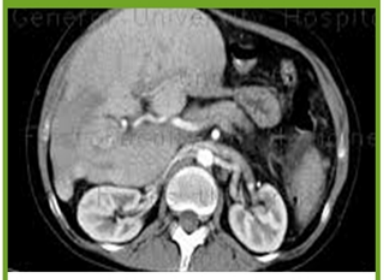
Jaundice, severe anemia, exchange transfusions

Toddlers, Children



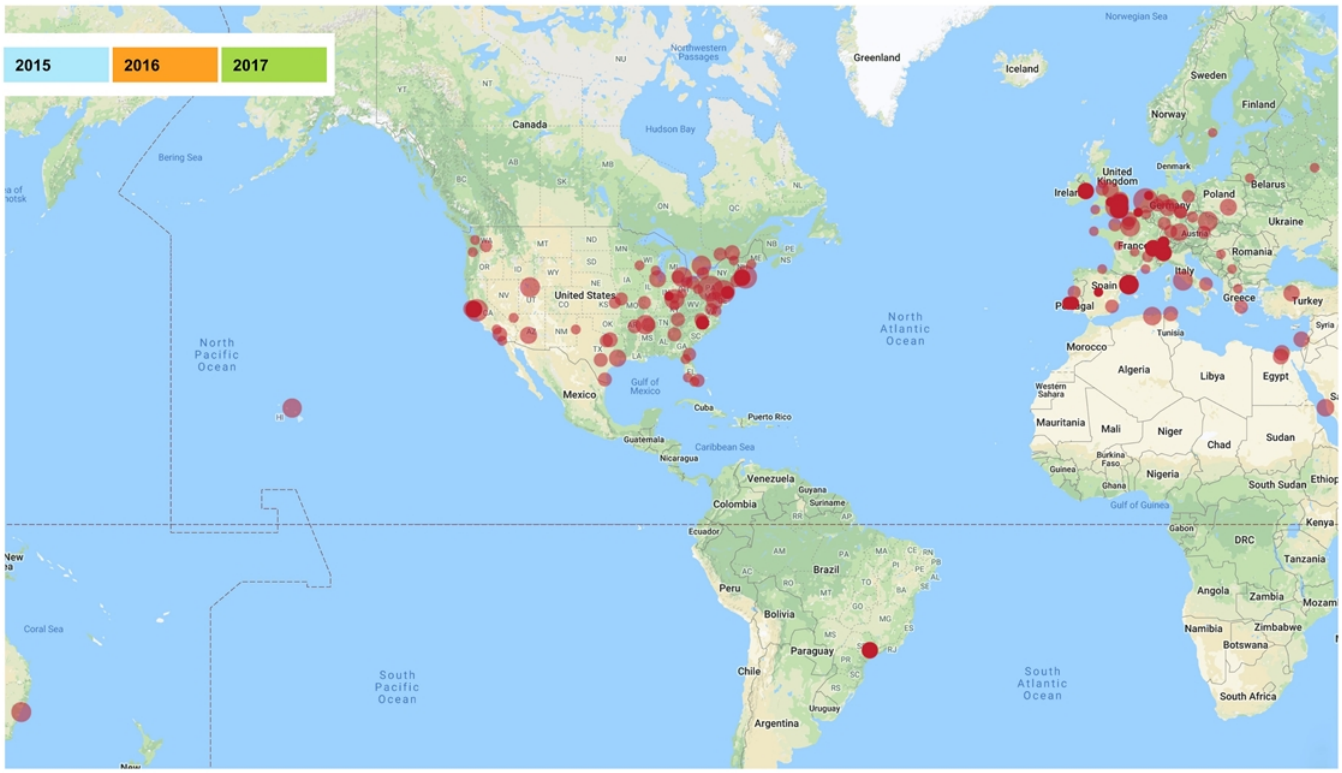
Splenectomy leading to increased infection risk, antibiotic prophylaxis

Adults

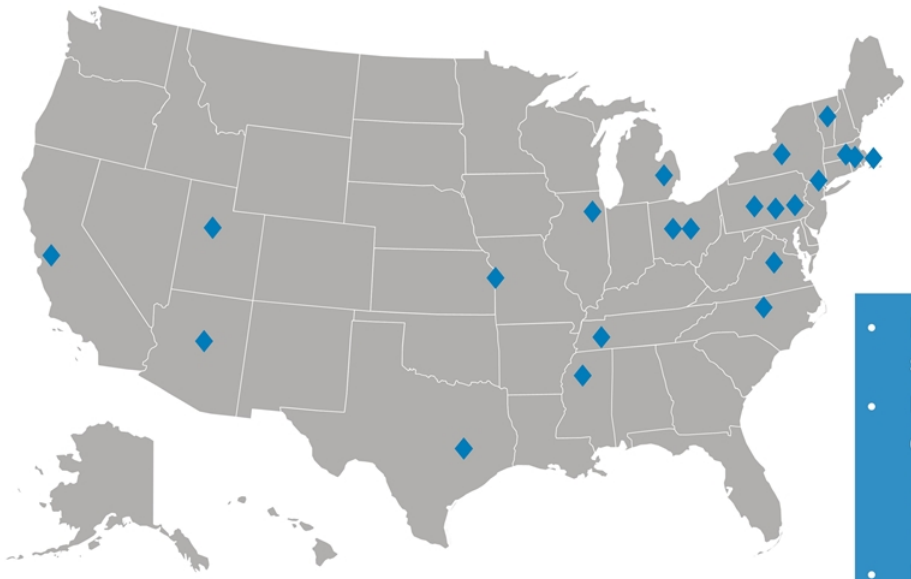


Iron overload leading to liver cirrhosis, cardiac and endocrine issues

Global Patient Finding Efforts



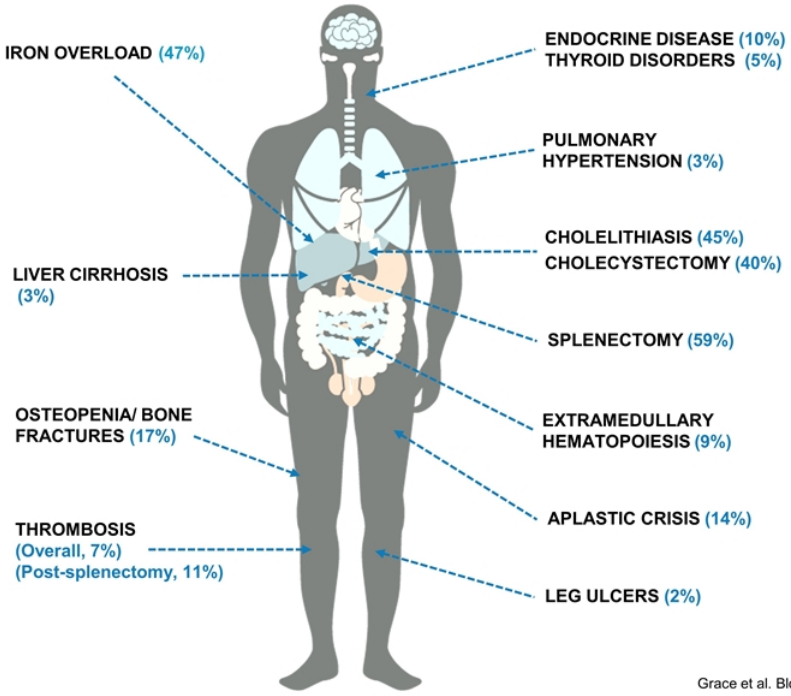
Boston Children's Natural History Study



- Initiated in 2014, 278 patients enrolled in 30 sites (North America & EU)
- Understanding symptoms and complications of the disease:
  - Transfusion burden
  - Incidence & timing of splenectomy
  - Prevalence & treatment of iron overload
- Identifying patients & treatment centers
- Identifying molecular characteristics

PK Deficiency: Burden of Disease is Extensive

Baseline and Retrospective Data from 254 NHS Patients



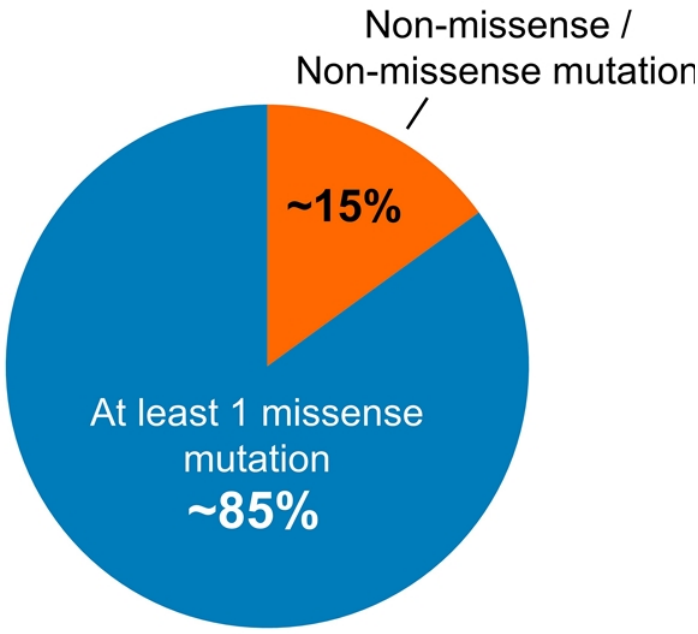
Grace et al. Blood, prepublished online March 16, 2018

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*

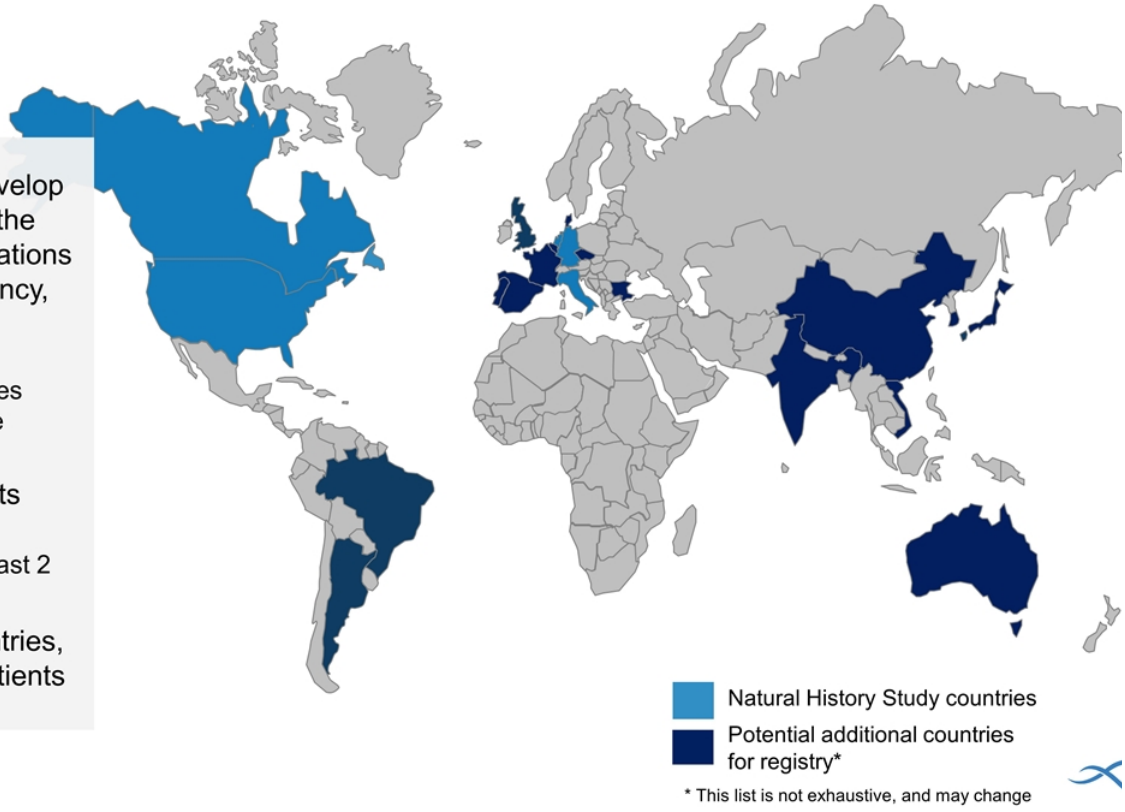
2. **Non-missense mutation** any mutation other than a missense mutation (*e.g.*, stop, frameshift, deletion) – *generally little functional protein*



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

PEAK Registry Enrolling Patients

- Primary objective is to develop greater understanding of the longitudinal clinical implications of pyruvate kinase deficiency, including:
  - Natural history
  - Treatments and outcomes
  - Variability of clinical care
  - Disease burden
- Adult and pediatric patients eligible
  - Will be followed for at least 2 years
- Will include up to 20 countries, 60 sites and up to 500 patients



ClinicalTrials.gov Identifier: NCT03481738

Physician Opinion of Disease Severity is Highly Variable and a Function of Patient Experience

Hematologists specializing in benign heme diseases are most familiar

PK deficiency patients are characterized by the overall disease burden

- Anemia
  - Iron overload, splenectomy, cholelithiasis
- Reduced stress response to viral infections, pregnancy
- Worsening symptoms with age

Significant gaps need to be addressed in the adult PK deficiency patient population

- Age characteristics of common complications, disease course, prognosis
- Risk factors for complications or for overall disease severity

Source: Agios PKD KOL advisory board, November 2017

Patients Describe a Constellation of Signs and Symptoms That Challenge Their Efforts to "Be Normal"

"I know more about my disease than my hematologist."

Living with PK deficiency

Physical burden | **Financial burden** | **Emotional burden**

- Disease impact increases as patients age
- Adequate health insurance
- Major life decisions (career, marriage, parenting) and everyday choices (travel, social life) affected
- Social QoL impact, not being able to "keep up"
- Bone pain, cognition impact, infections, iron overload, downstream co-morbidities / secondary conditions
- Anxiety about keeping disease private from employers

Caring for PK deficiency

- Relationships with HCPs vary widely
- No published standards of care
- Patients actively keep up with research to compensate for gaps in care & disease education
- Strong desire to participate in advocacy efforts & trials

Source: Agios 2017 patient advisory board

Agios PRO Tool Integrates Patient Perspective into Disease Burden

Assesses ***signs & symptoms*** and the ***impact on patients reported outcomes***

Signs & Symptoms	Physical limitations	Appearance	Daily life	Social impacts	Emotional impacts
• Fatigue / tiredness • Lack of / low energy • Exhaustion • Weakness • Dizziness / lightheadedness • Shortness of breath • Decreased stamina • Jaundice • Pale skin • Cognitive impairment • Bone pain • Joint pain	• Need for additional rest • Difficulty with exercise / sports • Difficulty with stairs / walking uphill • Susceptibility to illness	• Negative impact on appearance	• Difficulty with household activities • Lack of motivation • Less productive	• Negative impact on social activities • Negative impact on relationships with family/friends • Receiving unwanted attention	• Concern about the future

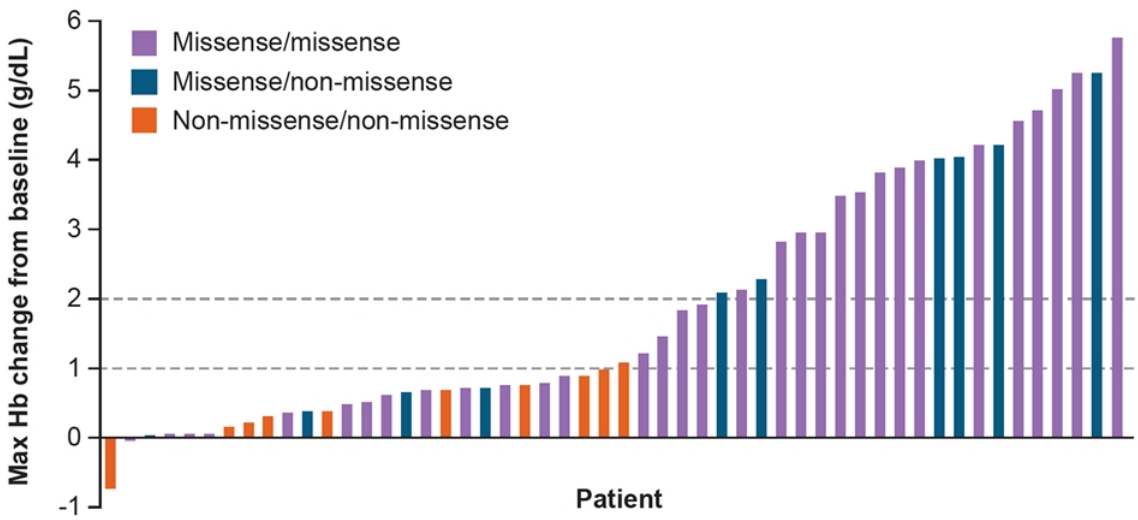
Endpoint in pivotal trials to evaluate treatment benefit

AG-348 Clinical Development Plan

Robust Hemoglobin Increases with AG-348 in DRIVE PK

- AG-348 continues to be well tolerated
- Measurements of hormone levels in men at doses ≤50 mg BID suggest mild aromatase inhibition

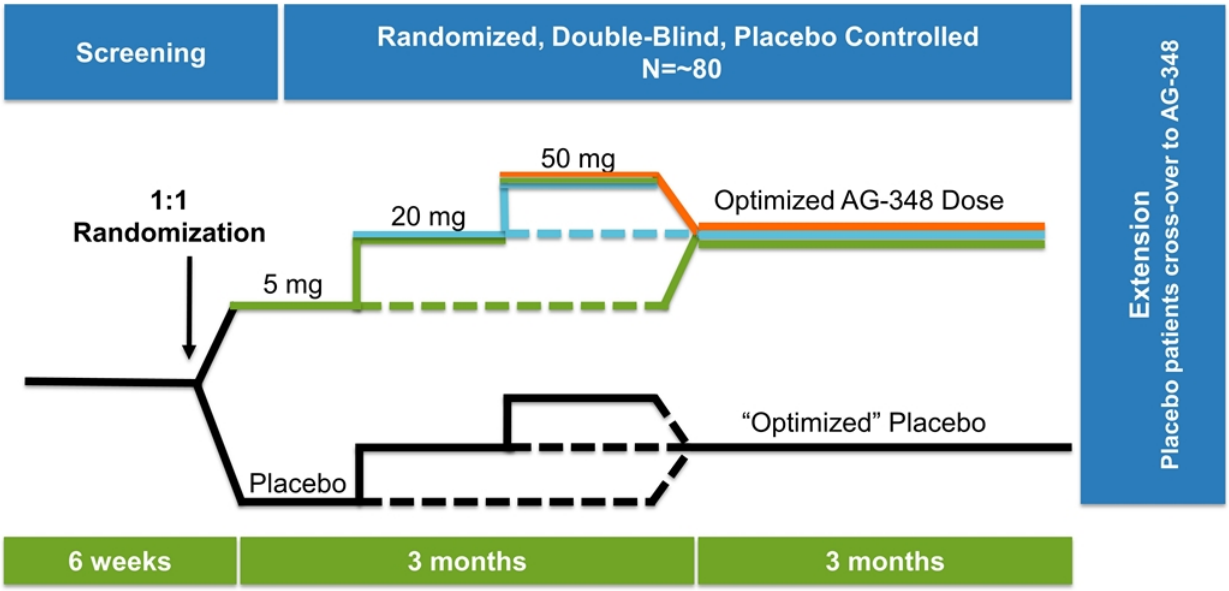
Maximum Hb increases observed by genotype



The baseline value is the average of all central assessments within the screening period (42 days prior to Day 1)

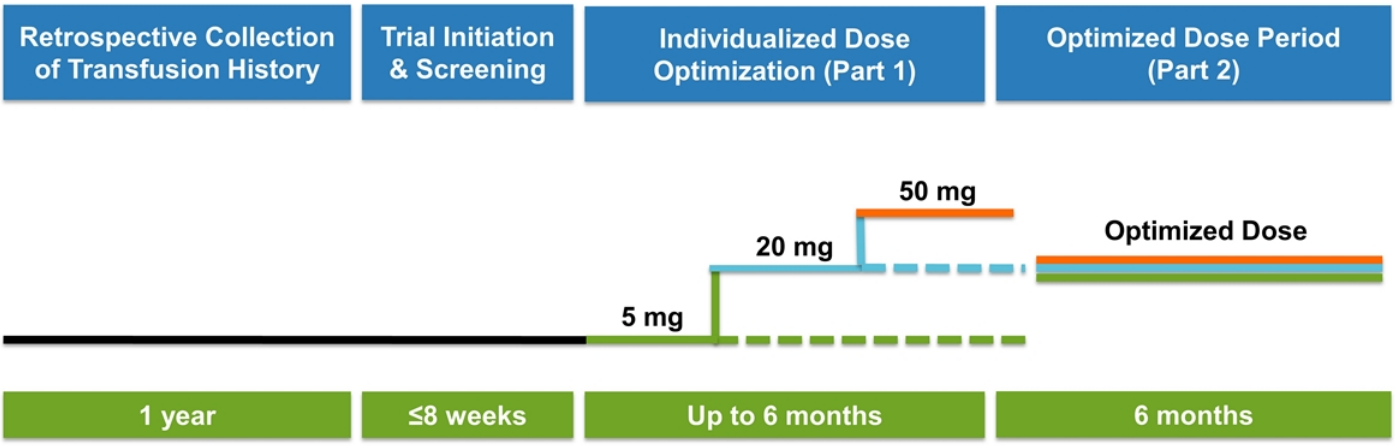
Source: Data presented at 2017 ASH Annual Meeting

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

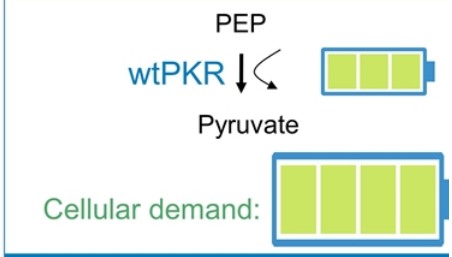
AG-348 ACTIVATE-T Trial for Regularly Transfused Patients



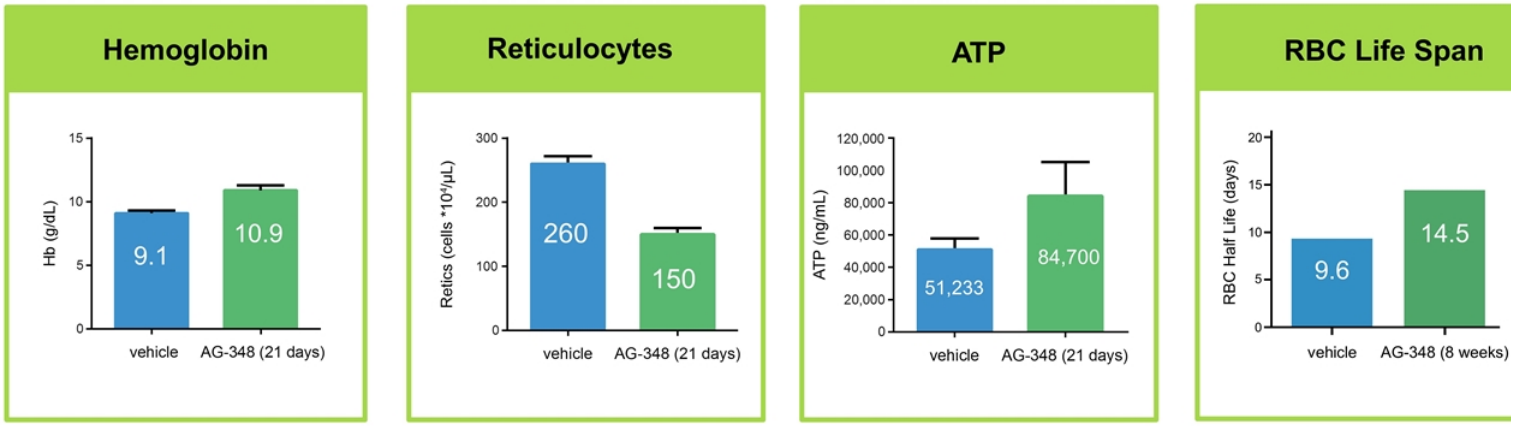
Approximately 20 regularly transfused patients who have required a minimum of 6 transfusions over the year preceding enrollment

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

PK Activation Represents Opportunities Across Hemolytic Anemias

Normal Red Cell	Pyruvate Kinase Deficiency	Other Hemolytic Anemias
		
ATP production meets demand	Inadequate production: ATP deficiency	Increased demand: ATP deficiency
	✓ Proof of concept achieved	**Thalassemia:** Expect to initiate Phase 2 proof-of-concept study in Q4 2018 **Sickle cell:** Planning underway

AG-348 Improves Red Cell Parameters in a Beta-thalassemia Mouse Model



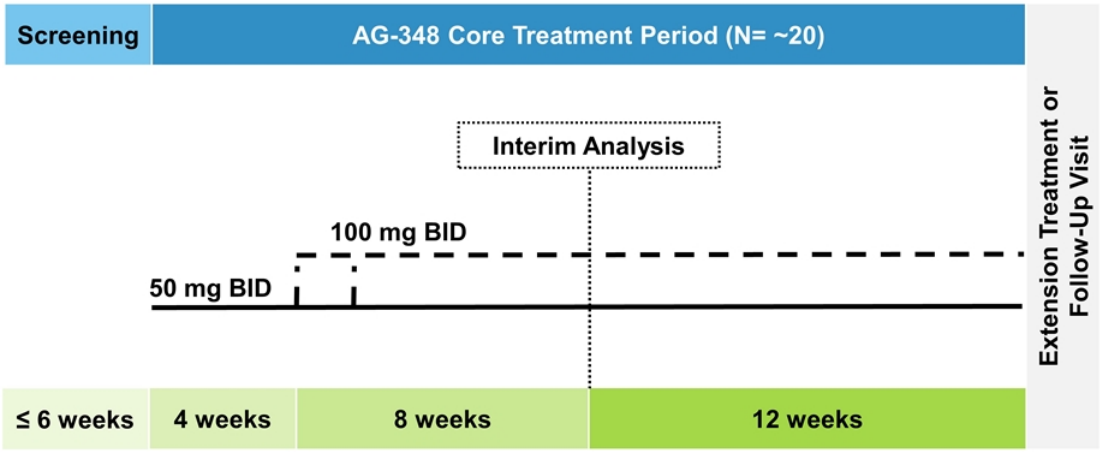
Vehicle
AG-348
(Hb, reticulocytes & A
days RBC half life, 8 v

- Treatment with AG-348 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

Source: Lucia de Franceschi, University of Verona

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



2,3-DPG Regulates Hemoglobin Oxygenation in Sickle Cell Disease

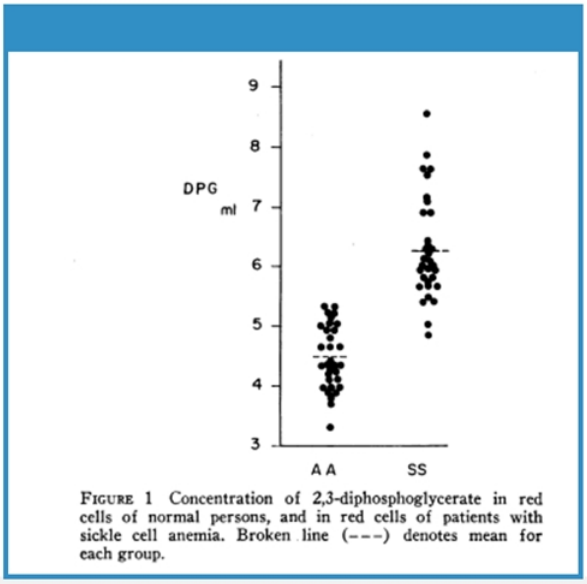
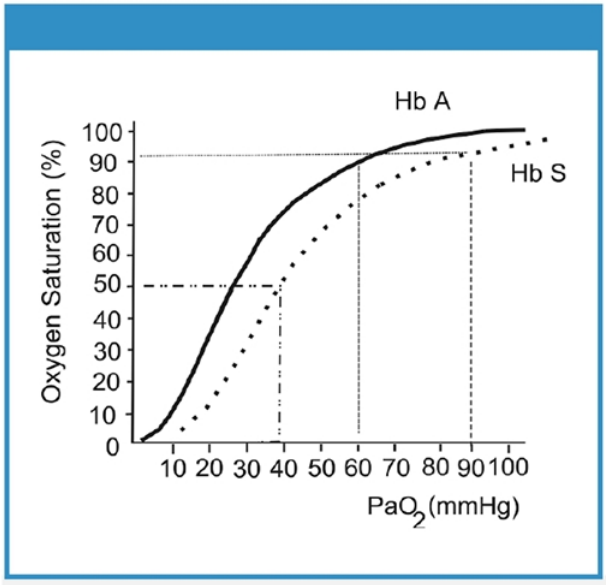


FIGURE 1 Concentration of 2,3-diphosphoglycerate in red cells of normal persons, and in red cells of patients with sickle cell anemia. Broken line (– – –) denotes mean for each group.

Sickle cells (SS) have higher 2,3-DPG compared to normal (AA)

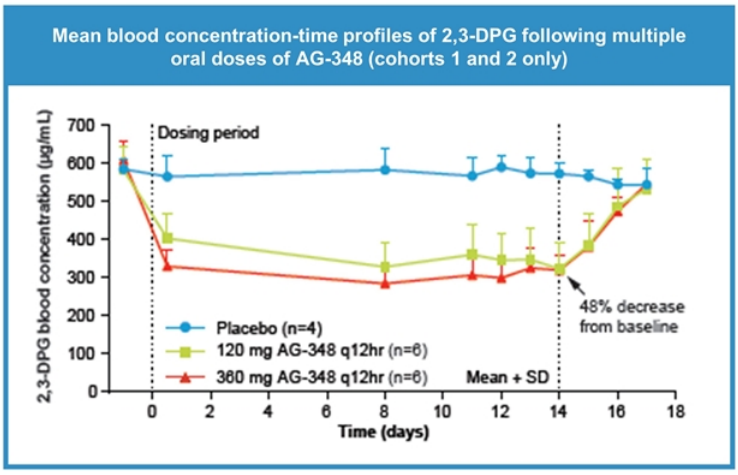


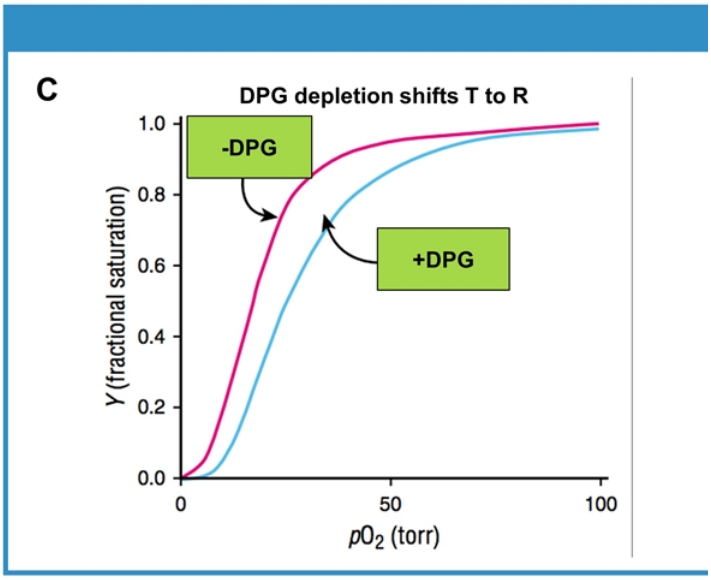
Decreased O_2 affinity can contribute to sickling in SCD
Same affinity for O2 in Sickle (Hb S) & normal (Hb A)

Sources: Journal of clinical sleep medicine JCSM, 3. 313-5;
L J Clin Invest. 1970 Apr; 49(4): 806–812

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





Sources: Agios 2016 EHA presentation, Eaton & Bunn, Blood, 2017

Defining the Potential for PKR Activation in Hemolytic Anemias

- Pyruvate Kinase Deficiency
  - Pivotal program underway for global registration
  - PEAK registry and Natural History Study will further define disease burden
- Life Cycle Expansion
  - Phase 2 proof-of-concept in Thalassemia to start 4Q'18
  - Planning for clinical development in sickle cell underway
    - Assessing biomarker endpoints and study designs for proof-of-mechanism and clinical concept
- Committed to investigating AG-348 in hemolytic anemias where PKR activation can help patients

Financial Overview & Q1 2018 Financial Results

Andrew Hirsch, Chief Financial Officer & Head of Corporate Development

Agios Approach to Drug Discovery and Development Drives Shareholder Value

Discovery Research

6 INDs in 8 years
7th planned for Q4 2018

- Discover new cancer or rare genetic disease targets or develop new biological insight to known pathway
- Rapidly validate the biology pre-clinically
- Develop small molecule chemistry to hit targets

Since 2009

Clinical Development

10+ clinical trials in 6 diseases

- Efficiently advance targets into clinic to attain proof-of-concept
- Aggressively expand therapeutic opportunity if mechanism warrants

Since 2013

Commercialization

1st medicine approved
2nd NDA under review

- Profitably commercialize each approved product

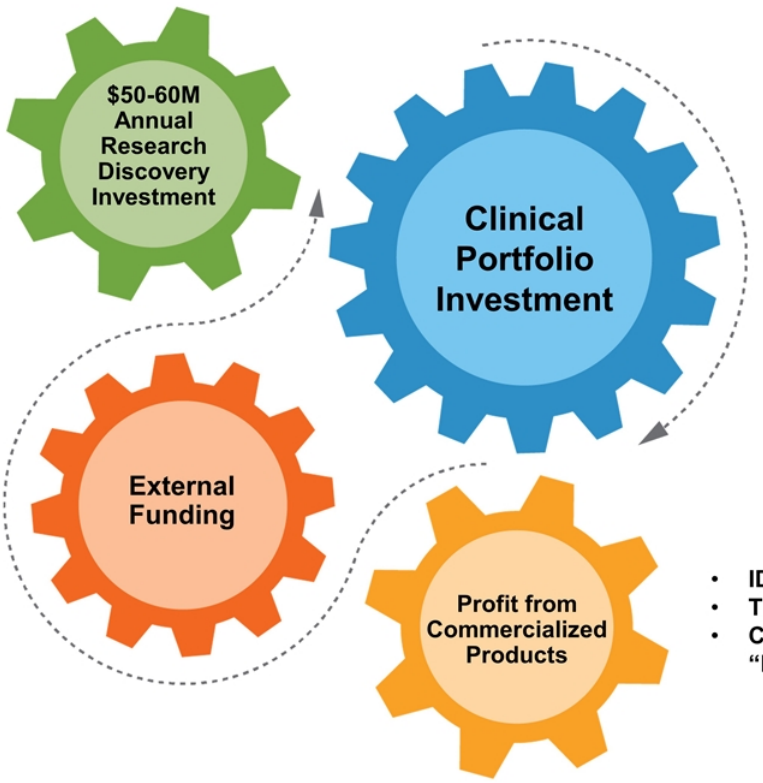
IDHIFA® (enasidenib) tablets 100mg • 50mg

TIBSOVO® (ivosidenib) tablets

Since 2017

Capital Formation and Investment Approach

- 6 INDs in 8 years
- 7th IND planned for Q4 2018
- 9 programs in late preclinical development

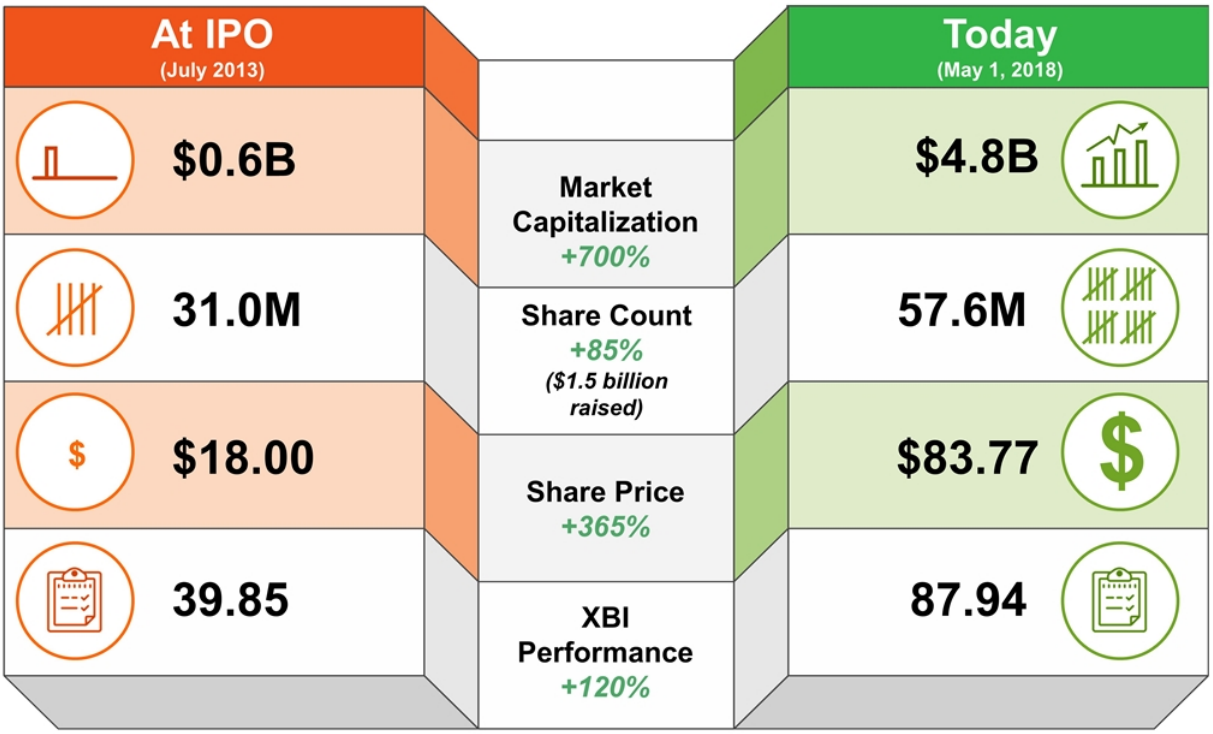


- IDHIFA NDA Approval <4 years from 1st patient dosed
- TIBSOVO® NDA under priority review
- 10+ clinical trials across 6 disea areas

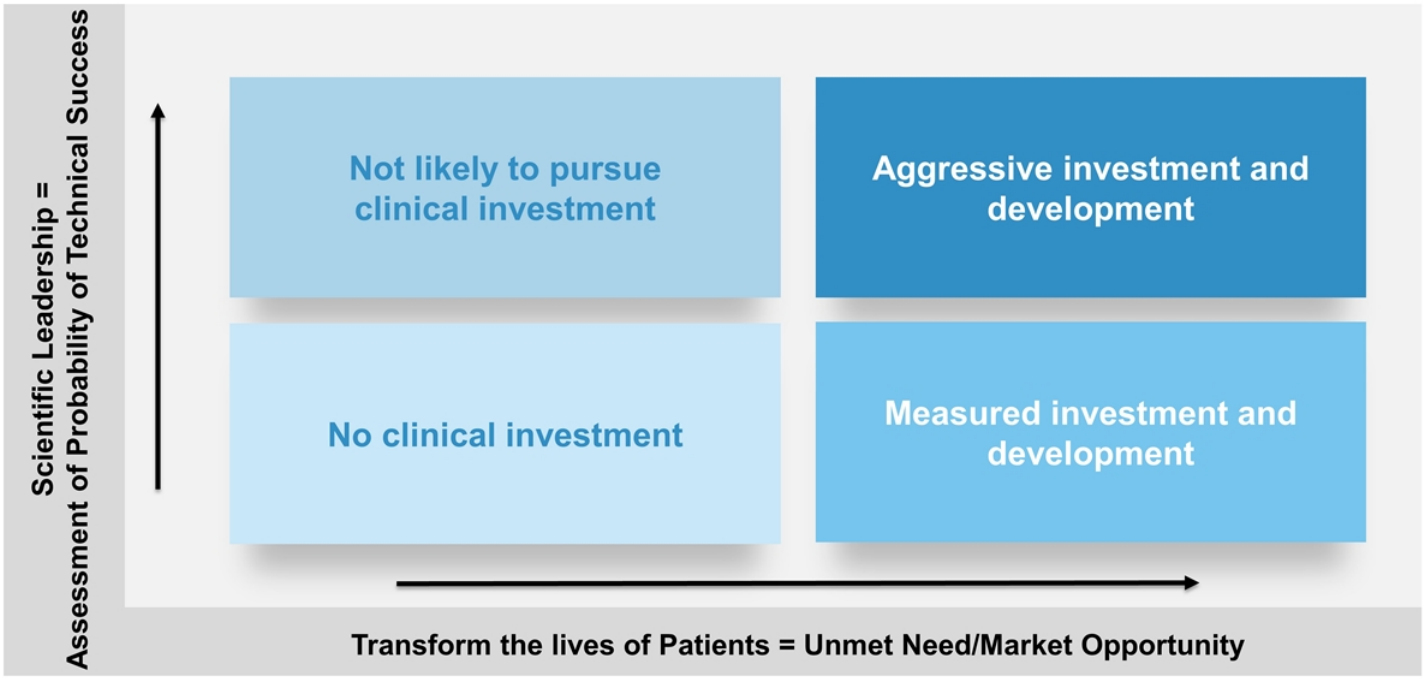
- ~$1.5 billion in equity raised from public markets
- ~$500 million received from Celgene collaborations

- IDHIFA royalty
- TIBSOVO® PDUFA date 8/21/18
- Commercial team in place and "launch ready"

Shareholder Value Creation Since IPO



Clinical Development Decisions Driven By Our Vision and Values



First Quarter Financial Results

Balance Sheet	March 31, 2018	December 31, 2017	Variance
Cash, Cash Equivalents and Marketable Securities	$995M	$568M	$427M
Total Assets	$1,040M	$614M	$426M

Statement of Operations	Three Months Ended March 31, 2018	Three Months Ended March 31, 2017	Variance
Collaboration Revenue	$7.3M	$10.5M	($3.2M)
Royalty Revenue	$1.4M	--	$1.4M
Research & Development Expense (1)	$78.2M	$62.7M	$15.5M
General & Administrative Expense	$24.6M	$14.8M	$9.7M

1) The R&D expenses reported for the three months ended March 31, 2017 are reported net of cost reimbursements of $2.8 million, for the three months ended March 31, 2018 cost reimbursements are reflected in Collaboration Revenue.

March 31, 2018 cash balance provides runway through at least the end of 2020

Q&A