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Q4 and Full Year 2022 Financial Results

February 23, 2023

Agios conference call participants

TOPIC	PARTICIPANT
Introductions	Jessi Rennekamp, Senior Director of Corporate Communications
Business Update	Brian Goff, Chief Executive Officer
Research & Development Update	Sarah Gheuens, M.D., Ph.D., Chief Medical Officer, Head of Research and Development
Commercial Update	Tsveta Milanova, Chief Commercial Officer
Fourth Quarter and Full Year 2022 Financial Results	Cecilia Jones, Chief Financial Officer
Q&A	Mr. Goff, Dr. Gheuens, Ms. Milanova, Ms. Jones

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 the potential benefits of PYRUKYND® (mitapivat), AG-946 and its PAH stabilizer; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND®, AG-946 and its PAH stabilizer; Agios' strategic vision and goals, including its key milestones for 2023 and potential catalysts through 2026; and the potential benefits of Agios' strategic plans and focus. The words "anticipate," "expect," "goal," "hope," "milestone," "plan," "potential," "possible," "strategy," "will," "vision," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Agios' current expectations and beliefs. For example, there can be no guarantee that any product candidate Agios 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, without limitation: risks and uncertainties related to the impact of the COVID-19 pandemic to Agios' business, operations, strategy, goals and anticipated milestones, including its ongoing and planned research activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products; Agios' results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA, the EMA or other regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; Agios' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials; unplanned cash requirements and expenditures; competitive factors; Agios' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; Agios' ability to maintain key collaborations; the failure of Agios to receive milestone or royalty payments related to the sale of its oncology business, the uncertainty of the timing of any receipt of any such payments, and the uncertainty of the results and effectiveness of the use of proceeds from the transaction with Servier; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' public filings with the Securities and Exchange Commission. Any forward-looking statements contained in this presentation and various remarks we make during this presentation speak only as of the date hereof, and Agios expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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Opening Remarks

Significant advances across our portfolio in 2022

FDA approval and launch of PYRUKYND® in adults with PK deficiency

Initiated the Phase 2a study of AG-946 in L-IR MDS

Initiated the SCD cohort of the AG-946 Phase 1 study

Initiated two Phase 3 studies of PYRUKYND® in pediatric patients with PK deficiency

Published clinical and translational data supporting the utility of PK activators across key disease areas and elucidating the burden of disease for PK deficiency, thalassemia and sickle cell

Closed screening in the Phase 2 portion of the RISE UP study of PYRUKYND® in adults with SCD

PYRUKYND® approved in adults with PK deficiency in EU and Great Britain

Enrolled a meaningful portion of patients in the ENERGIZE and ENERGIZE-T thalassemia studies

Q4 and full year 2022 highlights

Pipeline updates

- PYRUKYND® approved in U.S., EU, and Great Britain as the first and only disease-modifying therapy for PK deficiency
- Generated consistent and compelling data with PK activators in PK deficiency, thalassemia, sickle cell disease, and lower-risk MDS
- Advanced five pivotal clinical studies
- U.S. launch of PYRUKYND® providing a capability-building platform to support potential expansion in meaningfully larger patient populations

Corporate updates

- Made key appointments to management team
  - Brian Goff, CEO
  - Cecilia Jones, CFO
  - Tsveta Milanova, CCO
- Welcomed Dr. Rahul Ballal and Cynthia Smith to the Agios board of directors
- $1.1B in cash, cash equivalents, and marketable securities as of December 31, 2022

Clinical and regulatory milestones targeted in 2023 lay the foundation for transformational data readouts

Thalassemia PYRUKYND®	Complete enrollment of Phase 3 ENERGIZE and ENERGIZE-T studies (mid-year)
Pediatric PK Deficiency PYRUKYND®	Enroll at least half of patients in the Phase 3 ACTIVATE-kids and ACTIVATE-kidsT studies (year-end)
Sickle Cell Disease PYRUKYND®	Phase 2 RISE UP data readout & go/no-go to Phase 3 decision (mid-year)
Lower-Risk MDS AG-946 (Novel PK Activator)	Complete enrollment of Phase 2a study (year-end)
Pipeline	File IND for PAH stabilizer for the treatment of PKU (year-end)

Build commercial capabilities to efficiently launch additional indications and evaluate business development opportunities to expand pipeline

Potential for two additional PYRUKYND® indications by 2026

	2024	2025	2026
Thalassemia PYRUKYND®	Phase 3 ENERGIZE (1H) and ENERGIZE-T (2H) readouts	Potential approval	
Pediatric PK Deficiency PYRUKYND®		Phase 3 ACTIVATE-kids and ACTIVATE-kidsT readouts	Potential approval
Sickle Cell Disease PYRUKYND®		Potential Phase 3 RISE UP readout*	Potential approval
Lower-Risk MDS AG-946 (Novel PK Activator)	Phase 2a readout		

*Pending Go/NoGo decision in 2023

Driven to transform patient outcomes in rare diseases

2026 VISION


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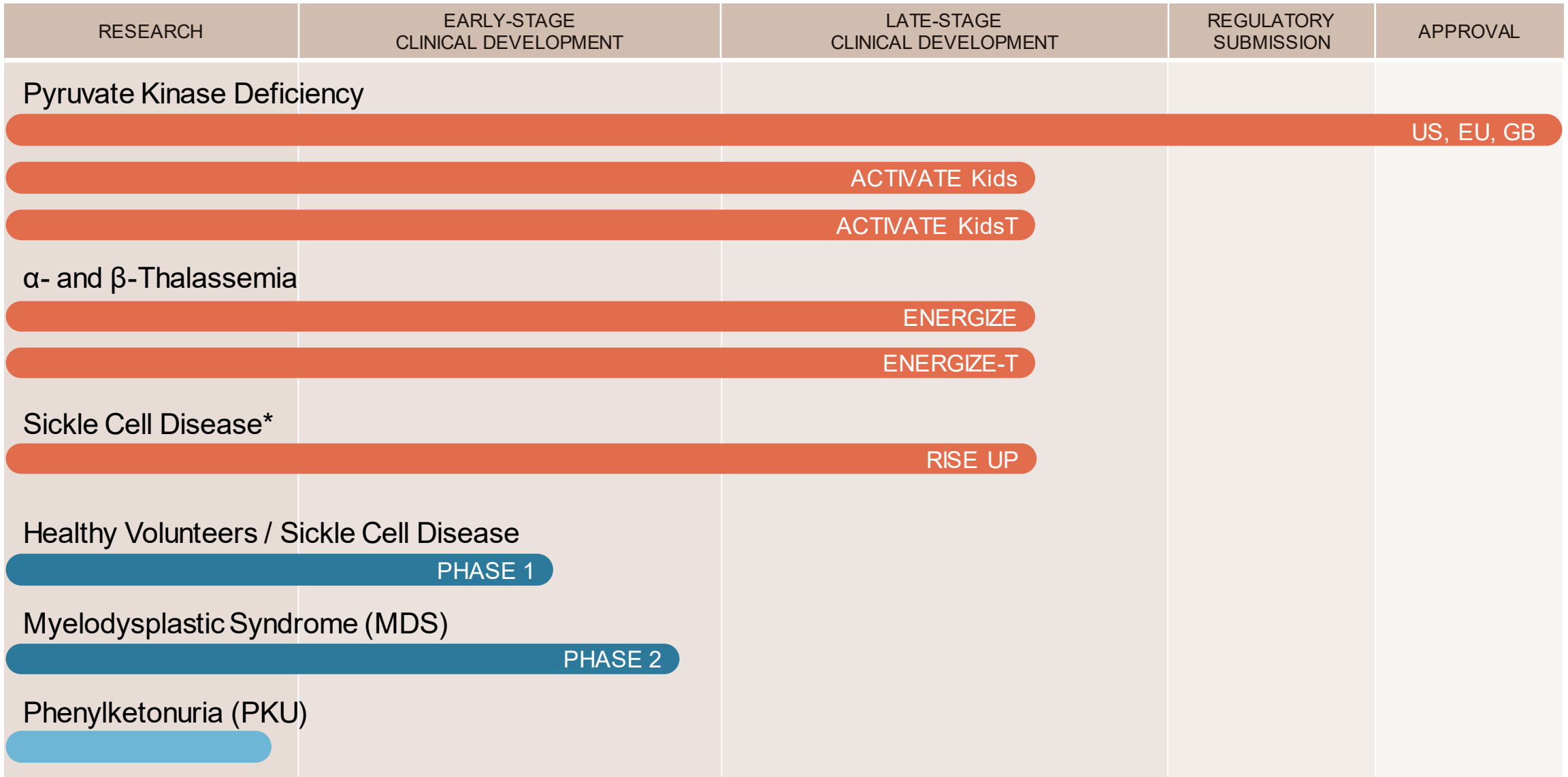
Building a diverse pipeline leveraging our expertise in cellular metabolism



*In addition to RISE UP, two investigator-sponsored trials are ongoing with the NIH and University of Utrecht.

PYRUKYND®
First-in-class PK activator

AG-946
Novel PK activator

Phenylalanine hydroxylase (PAH) stabilizer

Consistent and compelling data presented at ASH highlight potential of PK activators to transform patient function and quality of life across multiple therapeutic areas

American Society of Hematology Annual Meeting

December 10-13, 2022 | New Orleans, Louisiana

22 Agios and collaborator-led **presentations**

Updated long-term data from the thalassemia Phase 2 study

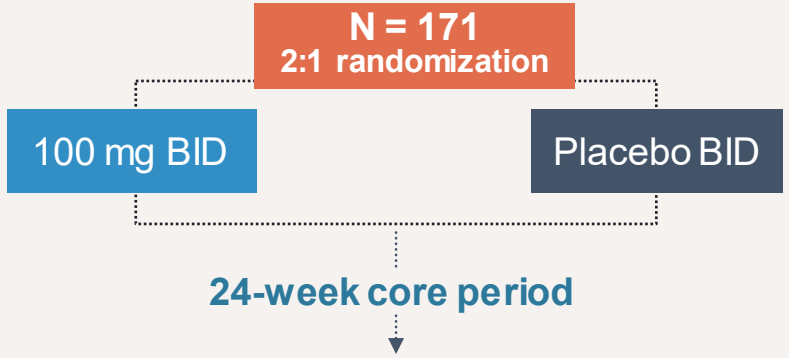
Updated long-term data from the PK deficiency Phase 3 extension study

Translational data spanning therapeutic areas of interest

AG-946 Phase 1 SAD/MAD **healthy volunteer data**

Two global, Phase 3, randomized controlled trials of PYRUKYND® in thalassemia encompass broad range of thalassemia patients

ENERGIZE



Primary endpoint

- Mean Hb ↑ ≥ 1 g/dL from baseline

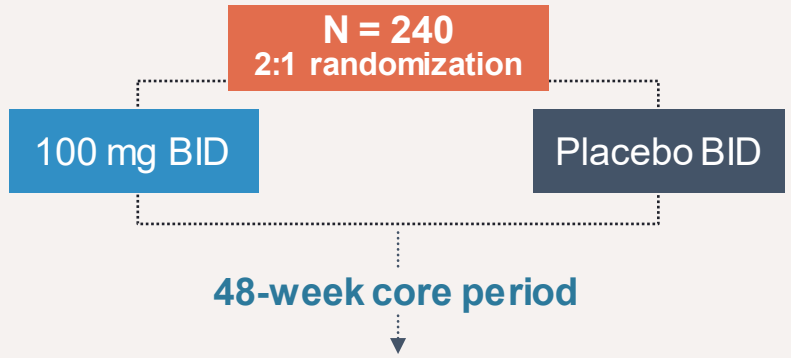
Secondary endpoints

- Fatigue, additional measures of Hb ↑, hemolysis, patient-reported outcomes, physical activity, iron metabolism, safety, PK/PD

Key inclusion criteria

- ≥ 18 years
- β-thalassemia ± α-globin mutations, HbE β-thalassemia, or α-thalassemia (HbH disease)
- Non-transfusion-dependent defined as ≤5 RBC units during the 24-week period before randomization and no RBC transfusions ≤8 weeks prior
- Hb ≤ 10.0 g/dL

ENERGIZE-T



Primary endpoint

- 50% reduction in transfusion burden in any 12-week rolling period

Secondary endpoints

- Additional measures of transfusion reduction, iron metabolism, safety, PK/PD

Key inclusion criteria

- ≥ 18 years
- β-thalassemia ± α-globin mutations, HbE β-thalassemia, or α-thalassemia (HbH disease)
- Transfusion-dependent defined as 6 to 20 RBC units transfused and ≤6-week transfusion-free period during the 24-week period before randomization

BID = twice daily; Hb = hemoglobin; HbE = hemoglobin E; HbH = hemoglobin H; PK = pharmacokinetics; PD = pharmacodynamics.

RISE UP Phase 2/3 operationally seamless trial of PYRUKYND® in sickle cell disease allows for speed and flexibility of clinical program

Evaluate totality of available data & external environment to trigger Phase 3 including:

Phase 2

- 1:1:1 randomization to mitapivat 50 mg BID, 100 mg BID or matched placebo
- N=69
- 12-week core period
- Primary endpoint:
- Safety and ≥1 g/dL ↑ in average Hb concentration from week 10 to 12 compared to baseline

PHASE 2 PRIMARY ENDPOINTS

Hemoglobin response	Safety profile

OTHER PHASE 2 DATA

Change in markers of hemolysis	Change in patient-reported fatigue
Annualized rate of sickle cell pain crises	PK/PD

COLLABORATOR-LED STUDIES

NIH Phase 1 extension	Utrecht Phase 2 ESTIMATE extension

OTHER AVAILABLE DATA

Phase 3

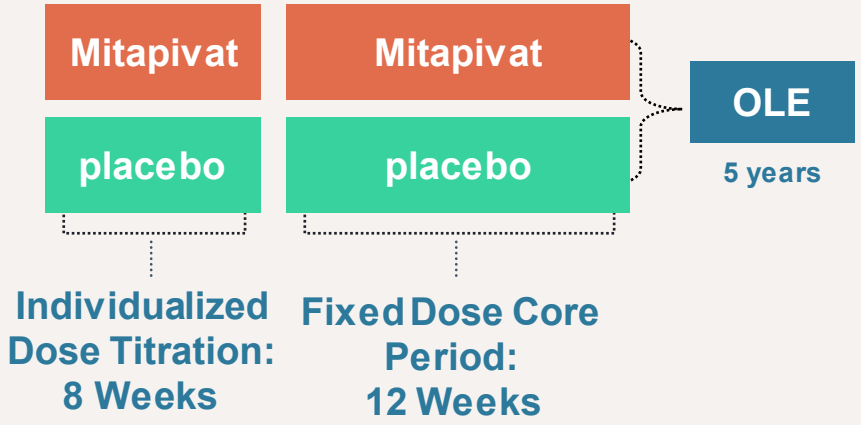
- 2:1 randomization to mitapivat Phase 2 dose or matched placebo
- N=198
- 52-week core period
- Primary endpoints:
- Mean Hb ↑ ≥ 1 g/dL from baseline & annualized rate of sickle cell pain crises

BID = twice daily; Hb = hemoglobin

Mitapivat development program in pediatric PK deficiency to support potential label expansion to those under 18

ACTIVATE-Kids™

Not Regularly Transfused PK Deficiency N=30
Randomize 2:1

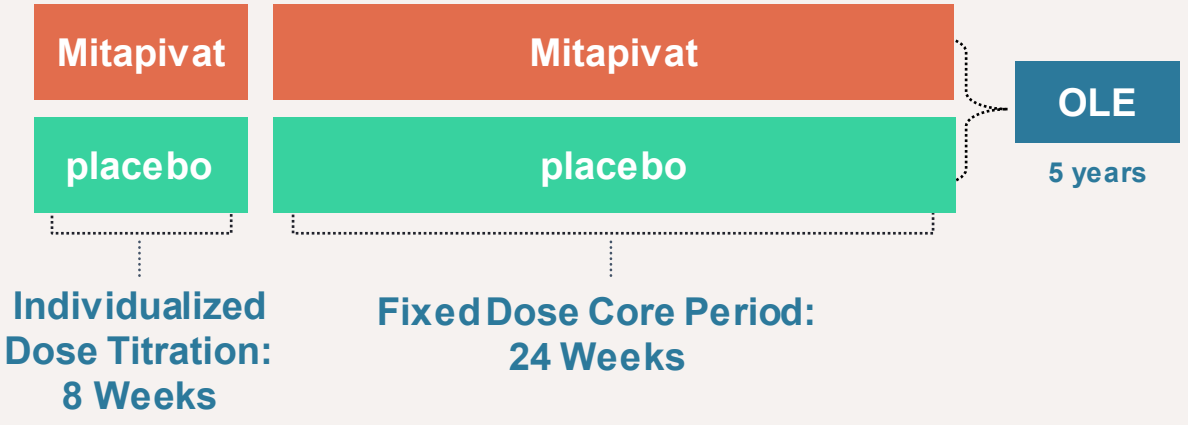


Eligibility

- 1 to <18 years of age
- Mean Hb concentration of ≤10 g/dL for patients 12 to <18 years or ≤9 g/dL for patients 1 to <12 years
- Not regularly transfused, with no more than five transfusions in the 12 months prior and no transfusions in the 12 weeks prior to the first day of study treatment

ACTIVATE-KidsT™

Regularly Transfused PK Deficiency N=45
Randomize 2:1



Eligibility

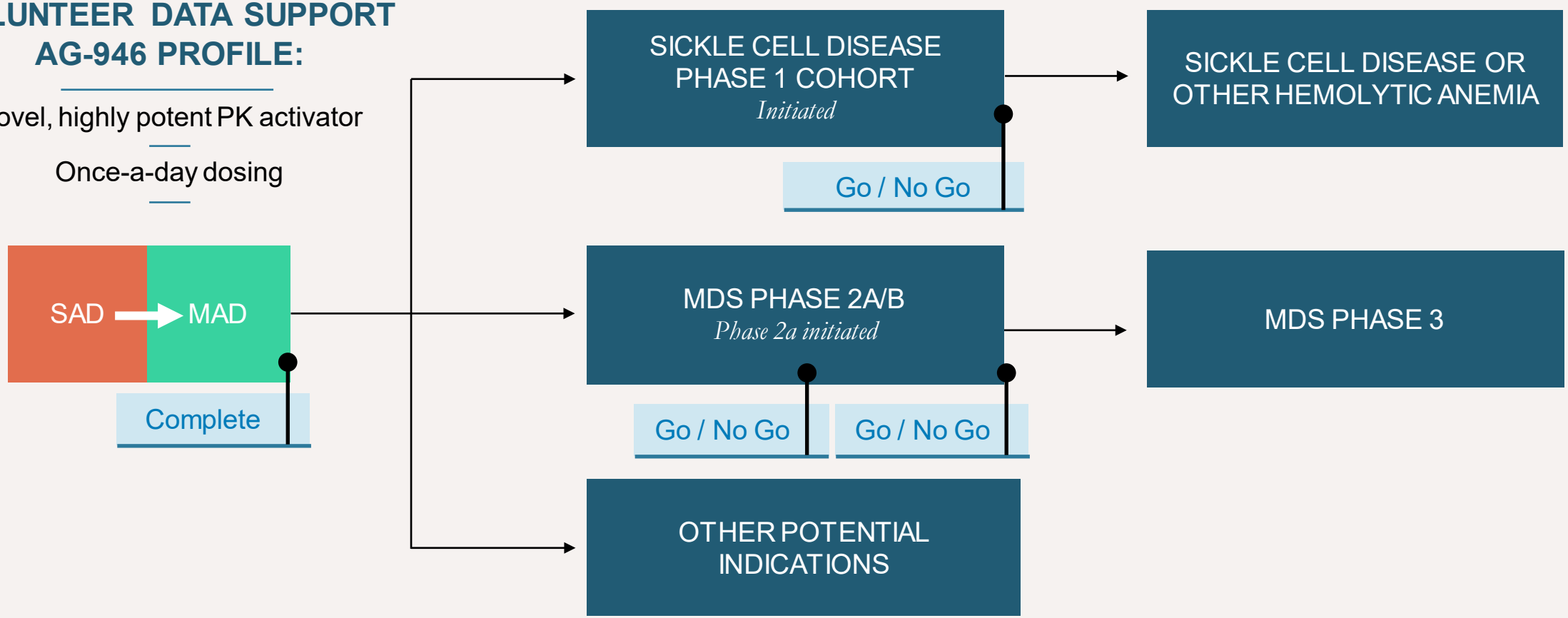
- 1 to <18 years of age
- Six to 26 transfusion episodes in the 52-week period before providing informed consent

Novel PK activator AG-946 provides opportunity to build on PYRUKYND® franchise and pursue multiple paths in parallel if data support advancement

PHASE 1 HEALTHY VOLUNTEER DATA SUPPORT AG-946 PROFILE:

Novel, highly potent PK activator

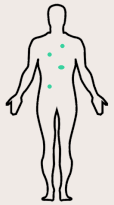
Once-a-day dosing



Source: ASH 2021

Lead research program aimed to address phenylketonuria (PKU)

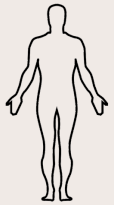
1



Normal Protein Diet

A mixed diet provides your body Phe

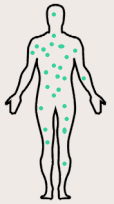
2



Defective PAH enzyme

PAH fails to process the Phe to Tyr

3



Increase in Phenylalanine

This leads to high Phe levels in the blood, which results in PKU

PHENYLKETONURIA (PKU)

- Rare, genetic disease with limited treatment options
- Prevalence: total of ~35-40K patients in the U.S. and EU5
- Driven by deficiency of phenylalanine hydroxylase (PAH) enzyme

AGIOS PROGRAM

- Oral PAH stabilizer designed to normalize phenylalanine levels
- Targeting IND filing by year-end 2023

Sources: National PKU Alliance, www.npkua.org and Weisbren et al 'Phenylalanine blood levels and clinical outcomes in phenylketonuria'; The American Journal of Human Genetics 107, 234–250, August 6, 2020; Agios internal estimates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Implementing a comprehensive commercial strategy that addresses each stage of the patient journey

Awareness

Increase disease awareness and educate on available treatment options

Access

Accelerate access by reducing the time between diagnosis and treatment initiation

Adherence

Support adherence and maintain reimbursement over the long term

Drive operational excellence in current launch and build capabilities for anticipated launches

PYRUKYND® Q4 2022 performance metrics highlight continued progress

$4.3M net U.S. sales of PYRUKYND®
for third full quarter of launch

78 patients on PYRUKYND®,
which includes new prescriptions and those continuing treatment, a 39% increase over Q3

Patients on therapy represent broad demographic range;
consistent with the adult PK deficiency population

105 unique patients completed PYRUKYND® prescription enrollment forms,
a 25% increase over Q3

Unique prescriber base of 96 physicians, diversified across the country

Near-term tactics to enhance focus on earliest stages of the patient journey

Awareness

Augment AI and machine learning capabilities for efficient physician targeting

Strengthen capacity for physician engagement and education

Increase disease awareness and diagnostic efficiency

PK activation franchise positioned for meaningful expansion, with near-term opportunity in thalassemia

PYRUKYND® is the first and only disease-modifying treatment approved for adults with PK deficiency

Potential for two additional PYRUKYND® indications by 2026

PK deficiency
Approved for adults in the U.S. and EU

3-8K patients
in the U.S./EU5

Thalassemia
Potential U.S. approval in 2025

18-23K patients
in the U.S./EU5

Sickle cell disease
Potential U.S. approval in 2026

120-135K patients
in the U.S./EU5

ADDITIONAL OPPORTUNITIES FOR THE FRANCHISE WITH NOVEL PK ACTIVATOR AG-946

Lower-risk myelodysplastic syndrome

75-80K patients
in the U.S./EU5

- Orphan patient populations
- High unmet need
- Focused prescriber pool
- Differentiated product profile

Source: Agios internal estimates


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Fourth quarter and full year 2022 financial results[1]

Statement of Operations	Three Months Ended 12/31/22	Three Months Ended 12/31/21	Year Ended 12/31/22	Year Ended 12/31/21
PYRUKYND® Net Revenue	$4.3M	--	$11.7M	--
Cost of Sales	$0.4M	--	$1.7M	--
Research & Development Expense	$70.3M	$73.3M	$279.9M	$257.0M
Selling, General & Administrative Expense	$32.8M	$31.5M	$121.7M	$121.4M
Gain on Sale of Oncology Business (TIBSOVO® Royalties)	--	$2.6M	$9.9M	$6.6M

Balance Sheet	12/31/22	12/31/21
Cash, Cash Equivalents and Marketable Securities	$1.1B	$1.3B

[1] Includes continuing operations on a comparative basis, which excludes results from divested oncology business.

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Closing Remarks

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Q&A