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Q3 2022 Financial Results

November 3, 2022

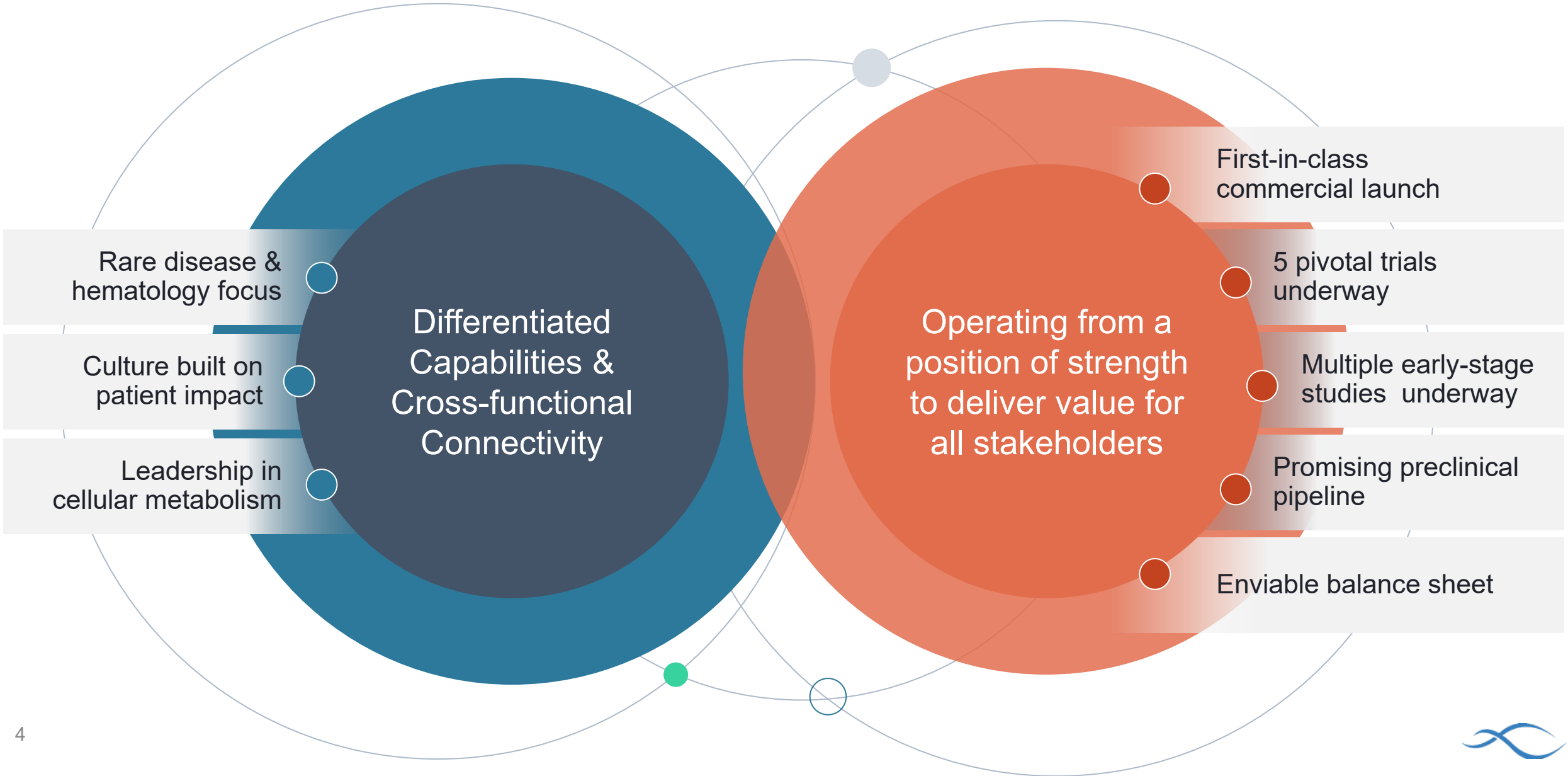
Agios conference call participants

TOPIC	PARTICIPANT
Introductions	Holly Manning, Senior Director of Investor Relations
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	Richa Poddar, Chief Commercial Officer
Third Quarter 2022 Financial Results	Cecilia Jones, Chief Financial Officer
Q&A	Mr. Goff, Dr. Gheuens, Ms. Poddar, Ms. Jones

Forward-looking statements

This communication 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 the preclinical, clinical and commercial advancement of its drug development programs, including PYRUKYND® (mitapivat) and AG-946; the potential benefits of Agios' products and product candidates; Agios' key milestones and guidance for 2022; its financial guidance regarding the period in which it will have capital available to fund its operations; 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. Management's expectations and, therefore, any forward-looking statements in this communication 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 on 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 future approved products, and launching, marketing and selling 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 and 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 establish and maintain 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, or SEC, including the risks and uncertainties set forth under the heading Risk Factors in our filings with the SEC. While the list of factors presented here is considered representative, this list should not be considered to be a complete statement of all potential risks and uncertainties. Any forwardlooking statements contained in this communication are made only as of the date hereof, and we undertake no obligation to update forward-looking statements to reflect developments or information obtained after the date hereof and disclaim any obligation to do so other than as may be required by law.

Strategy anchored to differentiated capabilities, creating a business operating from a position of strength



Meaningful Q3 and recent progress across the business

Pipeline progress

- U.S. PYRUKYND® net revenue $3.5M in Q3; launch learnings support capability building platform for future potential expansion
- Received positive CHMP opinion for PYRUKYND® in the EU
- Initiated the AG-946 MDS Phase 2a trial
- Published data from our thalassemia and PK deficiency clinical programs in the journals *Lancet* and *Lancet Haematology*, respectively
- Secured an expansive set of data for presentation at ASH in December

Corporate progress

- Monetized the TIBSOVO® royalty for receipt of a one-time payment of $131.8 million from Sagard Healthcare Partners
- Appointed Cecilia Jones to CFO
- Welcomed Dr. Rahul Ballal and Cynthia Smith to the Agios board of directors

Remaining milestones & priorities for 2022 key focus of Q4

FDA approval and launch of PYRUKUND® 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 PYRUKUND® 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

Complete enrollment in the Phase 2 portion of the RISE UP study of PYRUKUND® in adults with SCD *by year-end*

Potential EU and Great Britain approval of PYRUKUND® in adults with PK deficiency *by year-end*

Enroll a meaningful portion of patients in the ENERGIZE and ENERGIZE-T thalassemia studies *by year-end*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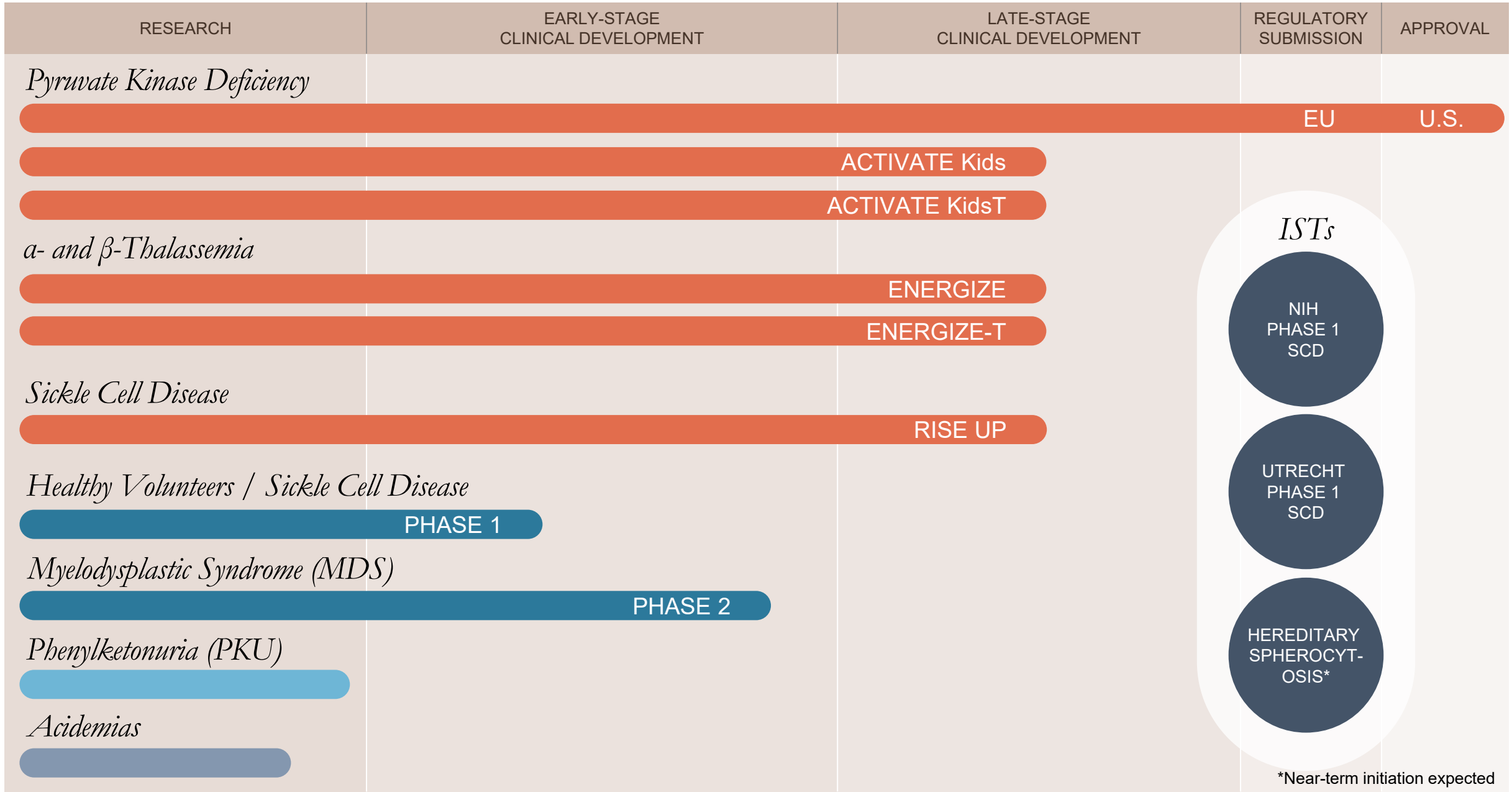
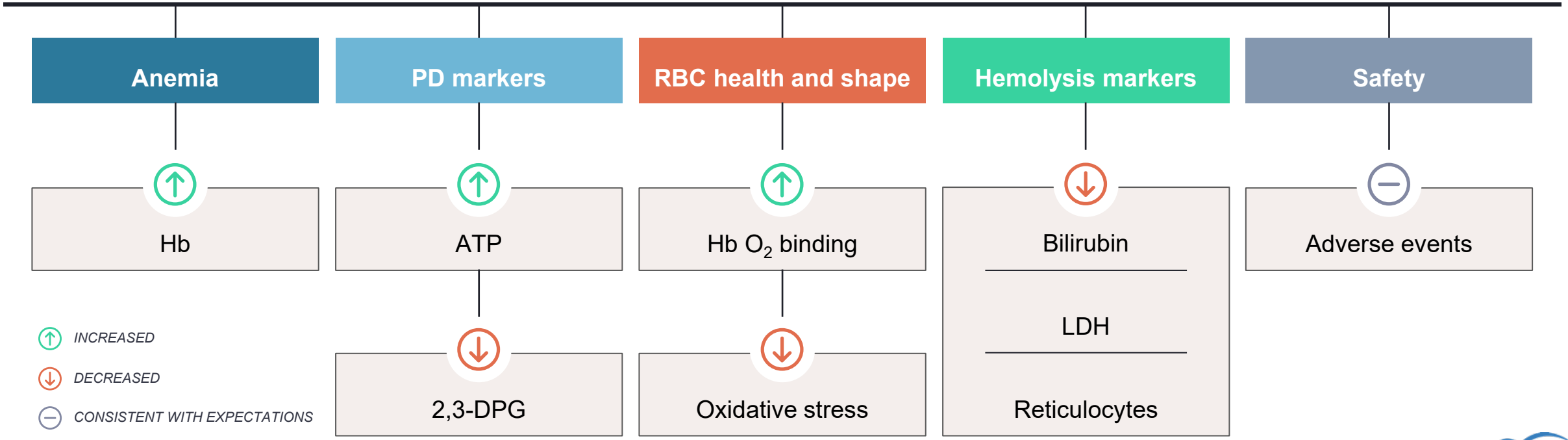

RESEARCH
EARLY-STAGE CLINICAL DEVELOPMENT
LATE-STAGE CLINICAL DEVELOPMENT
REGULATORY SUBMISSION
APPROVAL
Pyruvate Kinase Deficiency
EU
U.S.
ACTIVATE Kids
ACTIVATE KidsT
a- and β-Thalassemia
ENERGIZE
ENERGIZE-T
Sickle Cell Disease
RISE UP
Healthy Volunteers / Sickle Cell Disease
PHASE 1
Myelodysplastic Syndrome (MDS)
PHASE 2
Phenylketonuria (PKU)
Acidemias
ISTs
NIH PHASE 1 SCD
UTRECHT PHASE 1 SCD
HEREDITARY SPHEROCYT-OSIS*
*Near-term initiation expected
PYRUKYND® First-in-class PK activator
AG-946 Novel PK activator
Phenylalanine hydroxylate (PAH) stabilizer
Branched chain amino acid aminotransferase-2 (BCAT2) inhibitors

With more than 7 years of clinical experience and the largest dataset for any PK activator, PYRUKYND® demonstrated consistent results across 3 distinct diseases

Agios has pioneered the class of PK activators to transform the course of hemolytic and MDS-related anemia by increasing cellular energy to improve RBC development, health and longevity

PK Deficiency | Thalassemia | Sickle Cell Disease

POTENTIAL TO ADDRESS LONG-TERM COMPLICATIONS SUCH AS IRON OVERLOAD AND BONE MINERAL DENISITY



Sources: PYRUKYND® U.S. prescribing information; Kuo KHM et al. Lancet 2022; 400: 493–501; NIH data ASH 2021; Utrecht data EHA 2022

Agios at ASH 2022: Data underscore impact of long-term treatment with PYRUKYND and unmet need across therapeutic areas

American Society of Hematology Annual Meeting

December 10-13, 2022 | New Orleans, Louisiana

20+ Agios and collaborator-led **presentations**

Updated long-term data from the thalassemia Phase 2

Updated long-term data from the PK deficiency pivotal studies

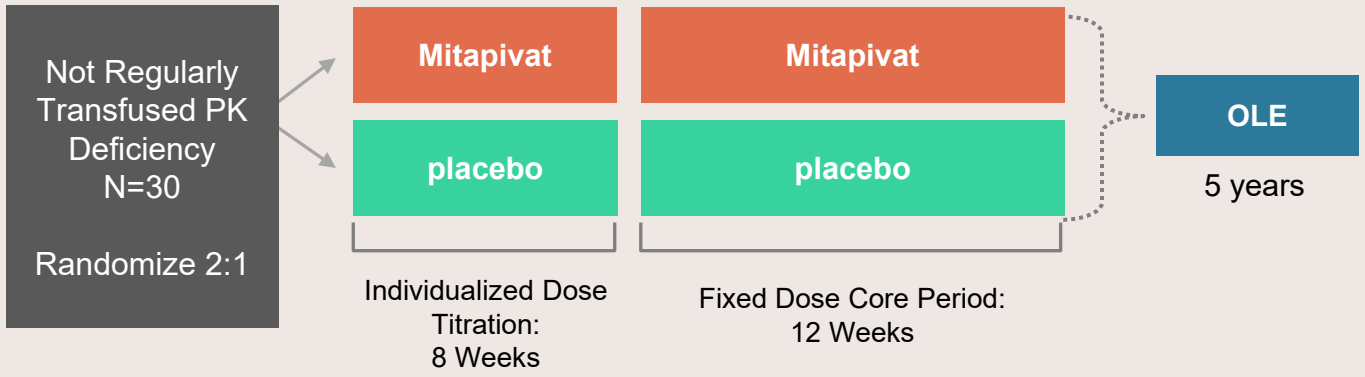
Translational data spanning therapeutic areas of interest

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

Abstracts go live today, November 3 at 9a.m. ET.

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

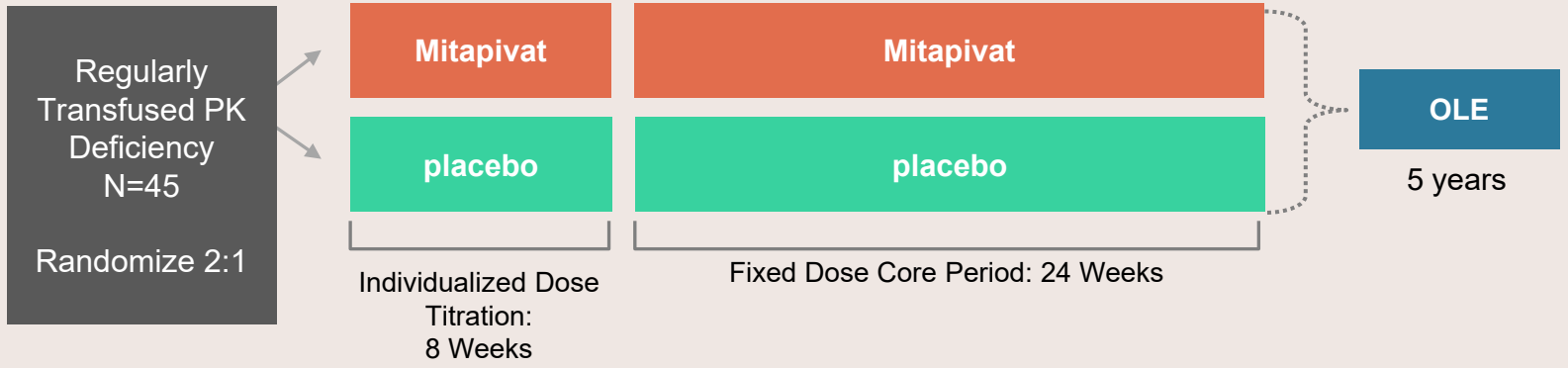
ACTIVATE-Kids™



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™



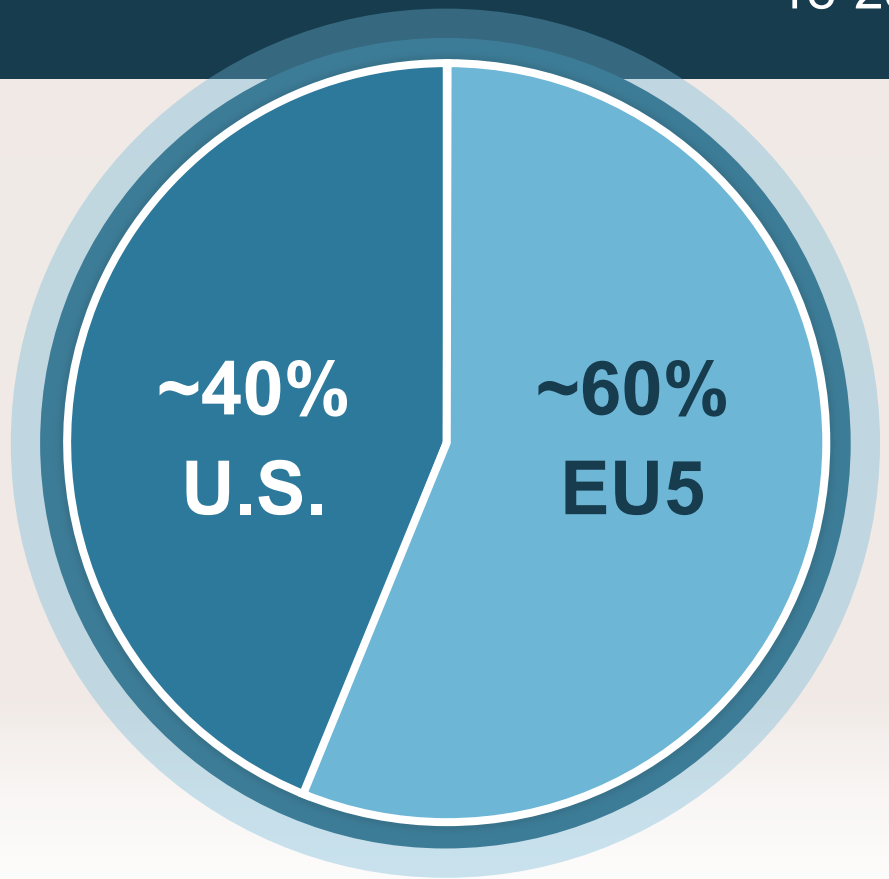
Eligibility:

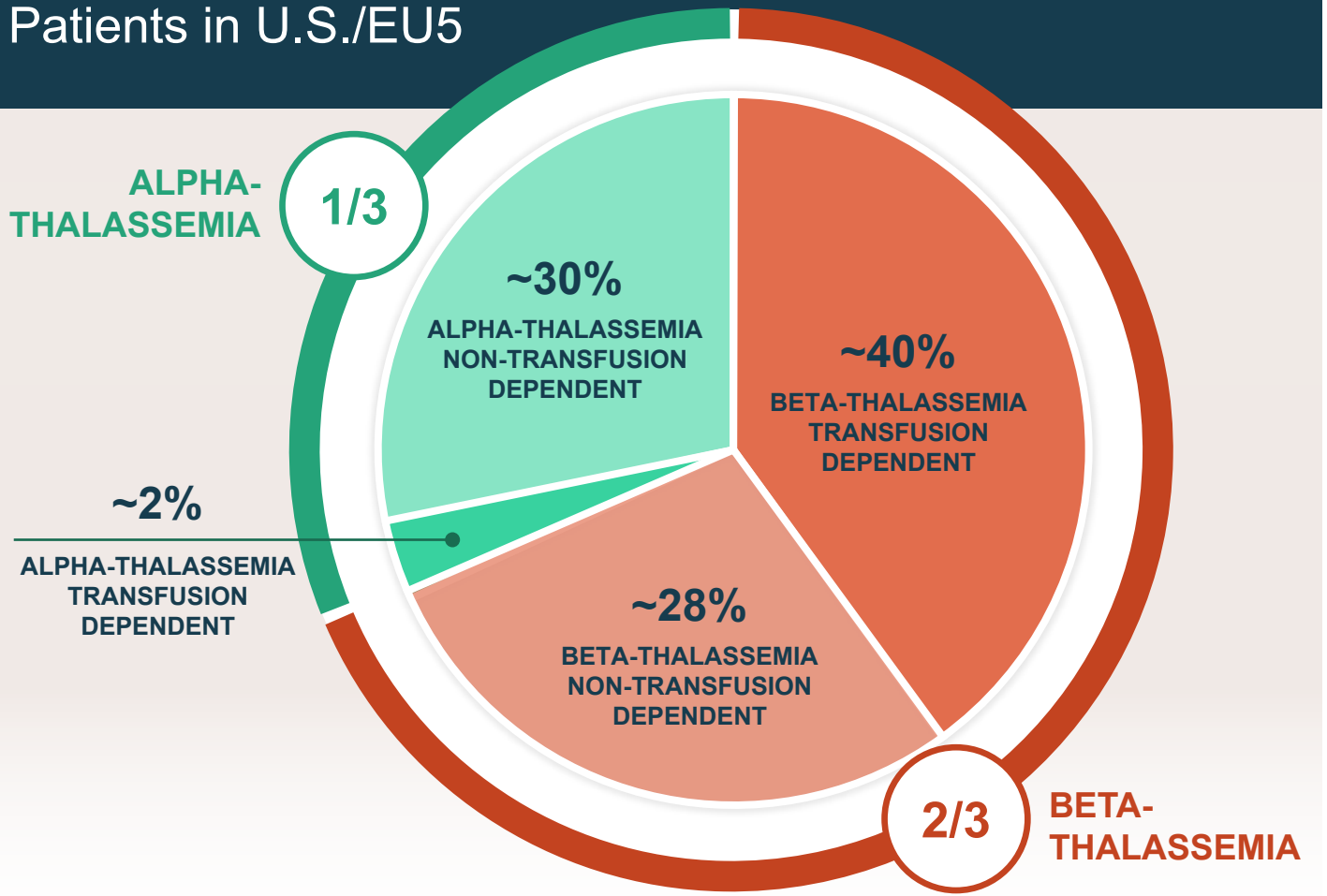
- 1 to <18 years of age
- Six to 26 transfusion episodes in the 52-week period before providing informed consent

Only transfusion dependent beta-thalassemia patients (~40% of all thalassemia) currently have an available treatment option

Thalassemia Patient Segments

~18-23K Patients in U.S./EU5

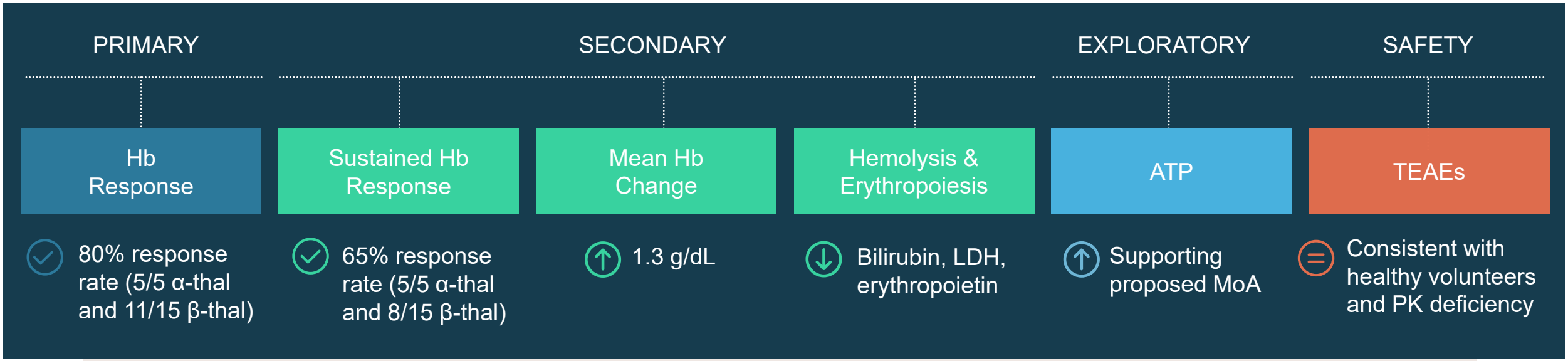




Beta-THAL prevalence: HEOR Global THAL Epidemiology SLE (XCENDA, 2021); US: Paramore, et.al; DE: Borchert, et.al; IT: Italian Society of Thal & Hemoglobinopathies Patient Registry, Jan 2021, Angelucci, et.al, 2017; FR: French registry for thal (Thuret, et.al.); ES: Cela, et.al.; UK Registry for Hemoglobinopathies, 2020
Alpha-THAL prevalence: Agios internal estimates; LEK Analysis | Beta-THAL TD/NTD split (60% / 40%): Thuret, et.al., Haematologica 2010; Magnolia TPP MR, April 2020 | Alpha-THAL TD/NTD split (5% / 95%): Taher, et.al., Vox Sanguinis, 2015; Magnolia TPP MR, April 2020

Data from Phase 2 study in non–transfusion-dependent α- and β-thalassemia support advancement of the ENERGIZE and ENERGIZE-T pivotal studies

Core period results:



17/20 patients entered long-term extension (LTE)

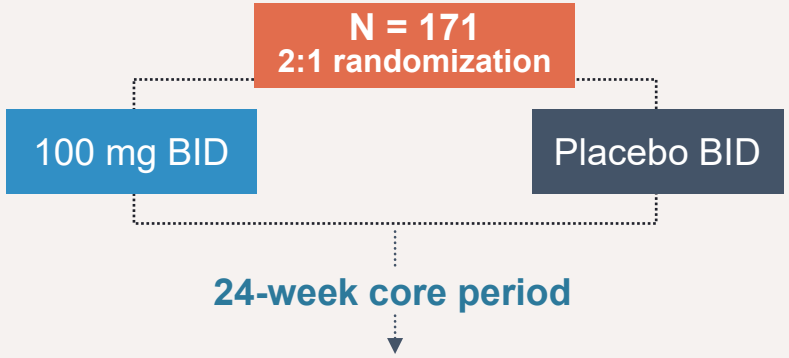
LTE data (median 70.9 weeks of treatment) presented at ASH 2021 showed sustained improvements in Hb, hemolysis and ineffective erythropoiesis and no new safety findings; updated data to be presented at ASH 2022

ATP = adenosine triphosphate; Hb = hemoglobin; LDH = lactate dehydrogenase; MoA = mechanism of action; PK = pyruvate kinase; PKR = PK in RBCs; TEAE = treatment-emergent adverse event.

Source: Kuo KHM et al. Lancet 2022; 400: 493–501; LTE data from ASH 2021

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

ENERGIZE



Primary endpoint

- Mean Hb ↑ ≥ 1 g/dL from baseline

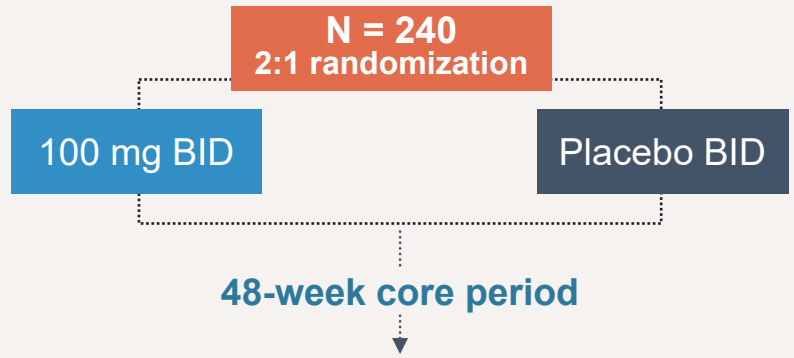
Secondary endpoints

- Safety, markers of hemolysis, patient-reported outcomes

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

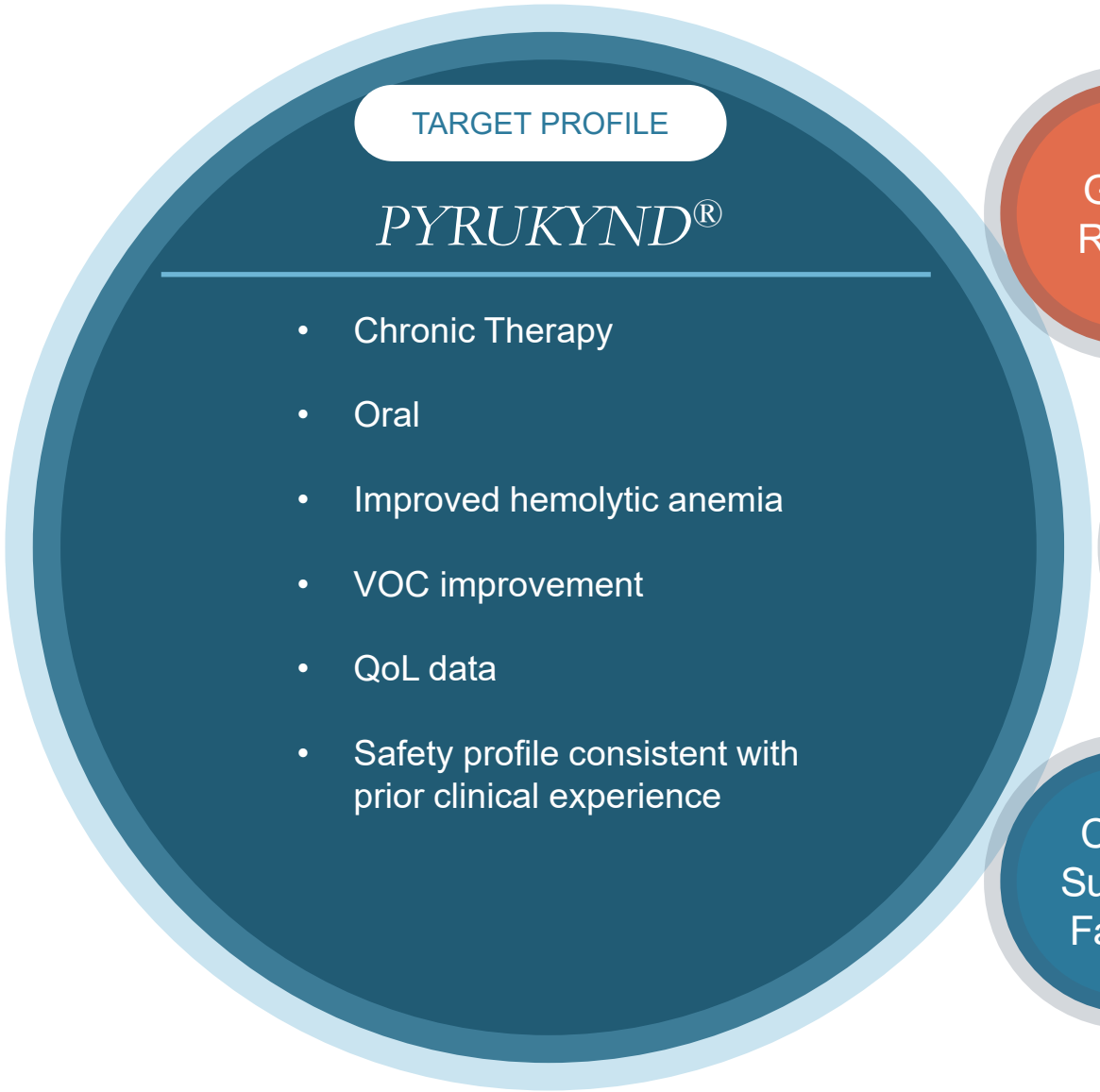
- Patient-reported outcomes, transfusion independence, markers of hemolysis, safety

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.

PYRUKYND® has potential to offer a holistic solution for the treatment of sickle cell disease (SCD)



Global Reach

- Estimated 120-135K patients across the U.S. & 5EU
- Significant opportunity outside of U.S./EU

Unmet Medical Need

- No approved therapy addresses both pain episodes and anemia

Critical Success Factors

- Innovative seamless Phase 2/3 trial RISE UP developed with community input
- Global approach to clinical development
- Connections with SCD patient and physician communities

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	Patient reported fatigue
Rate of sickle cell pain crises	Additional secondary endpoints

COLLABORATOR-LED STUDIES

NIH Phase 1 extension	Utrecht Phase 2 ESTIMATE extension

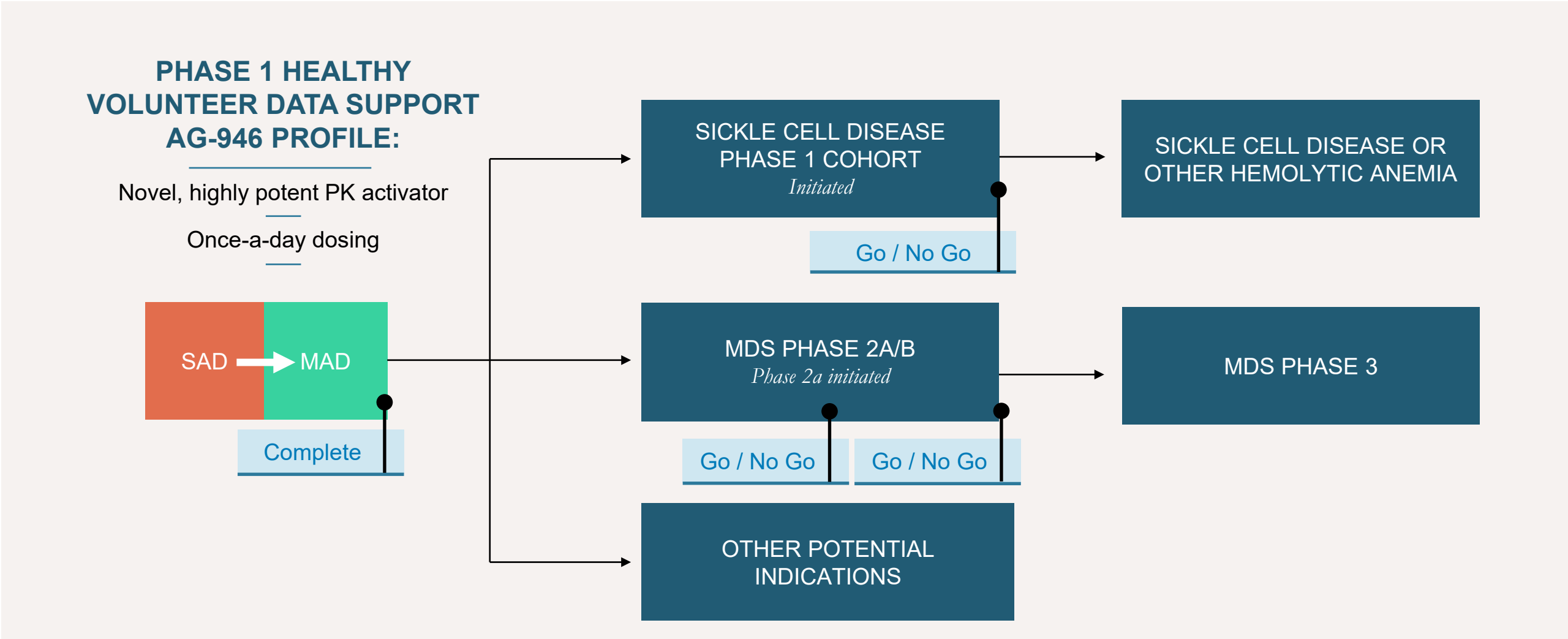
OTHER AVAILABLE DATA

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

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



Source: ASH 2021

PK activation has potential to address significant unmet need for effective therapies for lower risk MDS

MDS are a heterogeneous group of rare hematological malignancies characterized by ineffective erythropoiesis, abnormal cell maturation, dysplasia, and progressive cytopenias

- Approximately 50K patients in the U.S.
- Often characterized by anemia and red blood cell transfusion dependence
- Therapeutic strategies are limited for lower risk MDS anemia

PKR activator effects on ineffective erythropoiesis expected to translate to lower risk MDS, similar to thalassemia

- Potential to improve survival and differentiation of erythroid cells in bone marrow
- PKR activator improves RBC functionality by increasing ATP

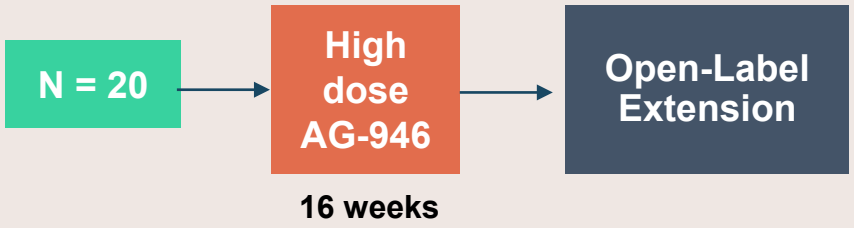
Acquired PK deficiency has been observed in MDS, suggesting that PKR may play a key role in MDS-associated anemia

- Strong clinical validation that activating PKR is beneficial when PKR is insufficient

Source: Agios internal estimates

Seamless Phase 2a proof-of-concept + Phase 2b trials of AG-946 focused on establishing proof-of-concept and dose selection in MDS

Phase 2a — Open Label

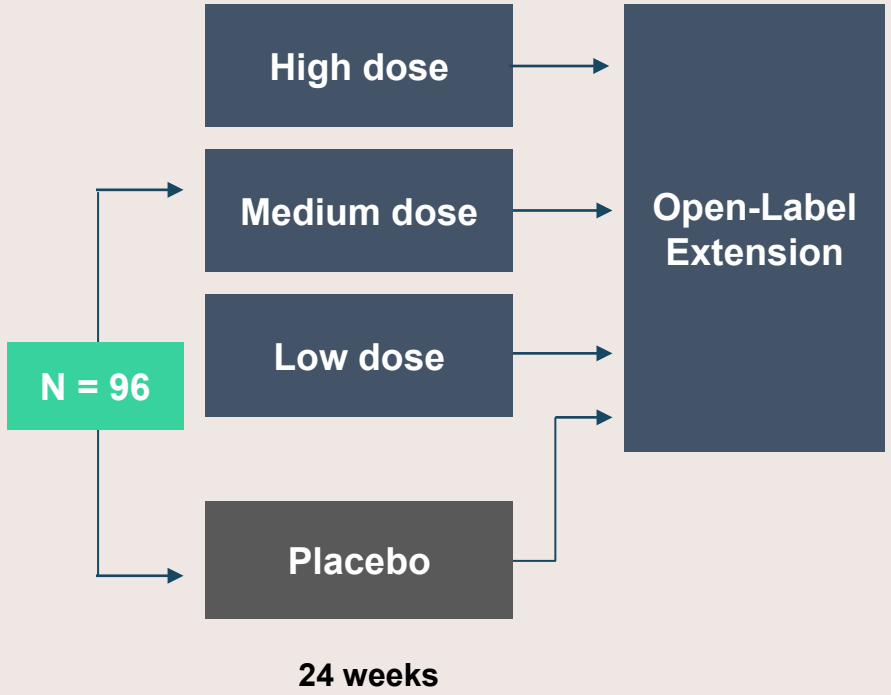


Primary endpoints:

- Hemoglobin (Hb) response, defined as a ≥1.5-g/dL increase from baseline in the average Hb concentration from Week 8 through Week 16
- Transfusion independence, defined as transfusion-free for ≥8 consecutive weeks during the Core Period (participants with low transfusion burden only)

Secondary endpoints: safety, additional measures of anemia, PK and PD biomarkers

Phase 2b — Double Blind, 1:1:1:1 Randomization

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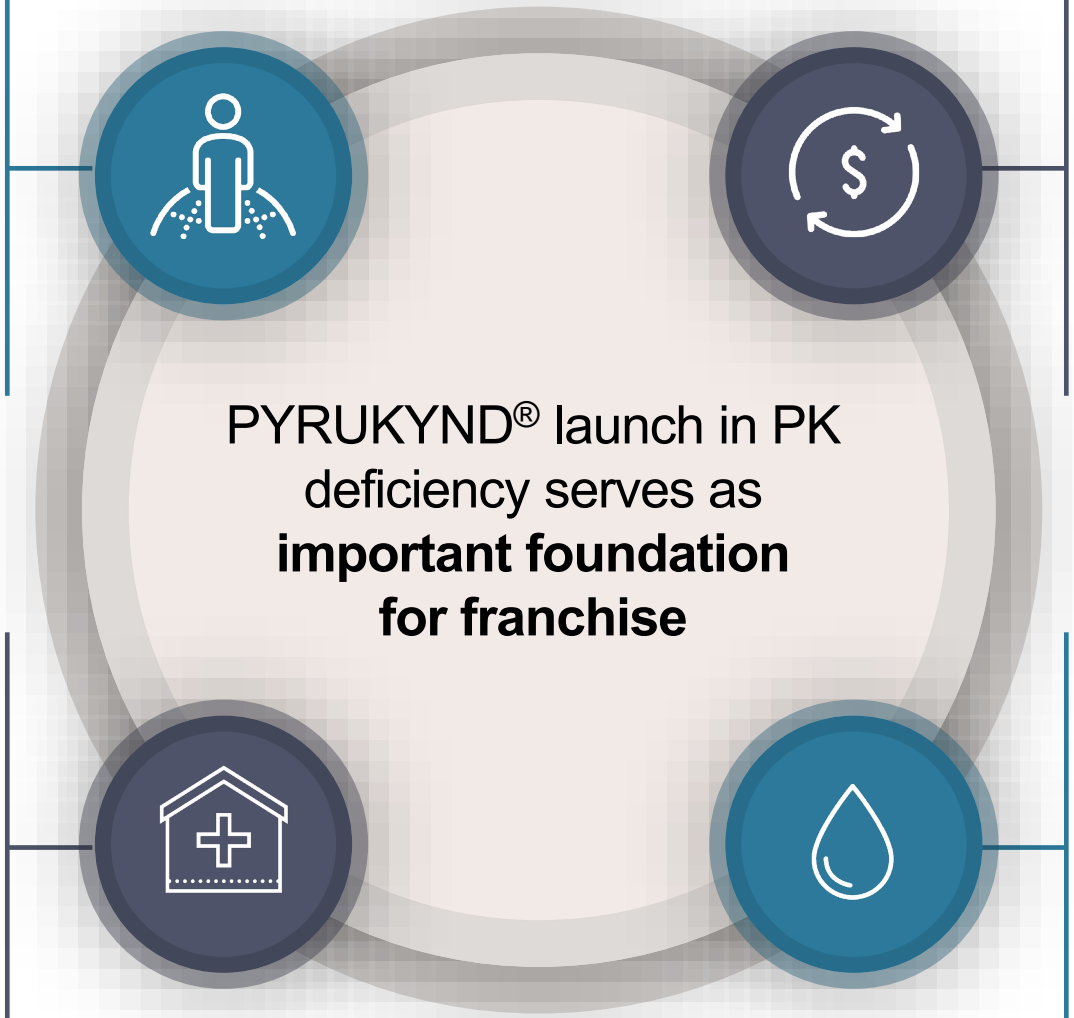
PATIENTS

First ever therapy for patients with PK deficiency – a game changer for this under-recognized, poorly understood disease

REVENUE

Modest but important revenue generator for the business

U.S. peak potential of $200-225M for PK deficiency alone



REAL-WORLD IMPACT

Serves as the first proof point for PYRUKYND® in the real world, uncovering the opportunities for the first PK activator on the market

CAPABILITY-BUILDING

First, PK deficiency pivotal trials honed our global rare disease and classical hematology clinical capabilities

Now, PYRUKYND® launch establishes our commercial platform in rare diseases and serves as introduction to the broader hematology community

PYRUKYND® Q3 2022 performance metrics highlight early launch health

$3.5M net U.S. sales of PYRUKYND®
for second full quarter of launch

56 patients on PYRUKYND®,
which includes new prescriptions and those continuing treatment, a 51% increase since Q2

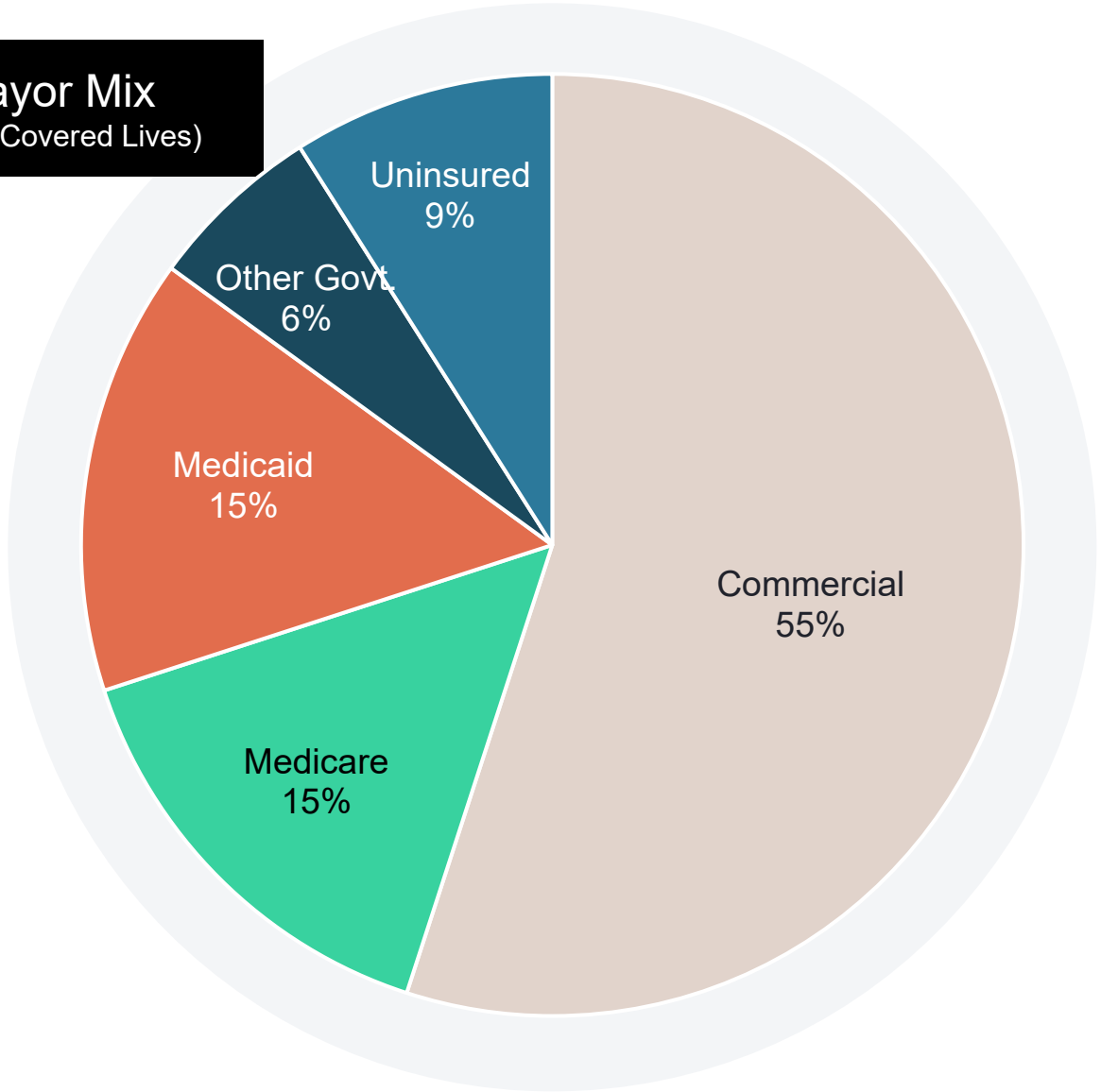
Patients on therapy represent range of demographics;
splenectomized/not splenectomized, young adults to elderly, baseline hemoglobin, transfusion status

84 unique patients completed PYRUKYND® prescription enrollment forms,
a 64% increase since Q2

Unique prescriber base of 80 physicians, diversified across the country

Effective payer engagement to ensure access for eligible patients

Payor Mix
(% Covered Lives)



- ✓ Payer mix aligns with expectations
- ✓ Payer policies across our payer segments are being developed
- ✓ Policies align to the indication statement or the clinical trial eligibility criteria as anticipated
- ✓ Prior authorization criteria align to rare, specialty medicine and typically include the need for genetic testing, consultation with a specialist, and baseline hemoglobin and transfusion history.

Free genetic testing program, Anemia ID, designed to encourage broad testing for patients with suspected hereditary anemia earlier in the diagnostic workup

As of Sept. 30:

More than 5,300 kits have been ordered, a 26% increase since Q2

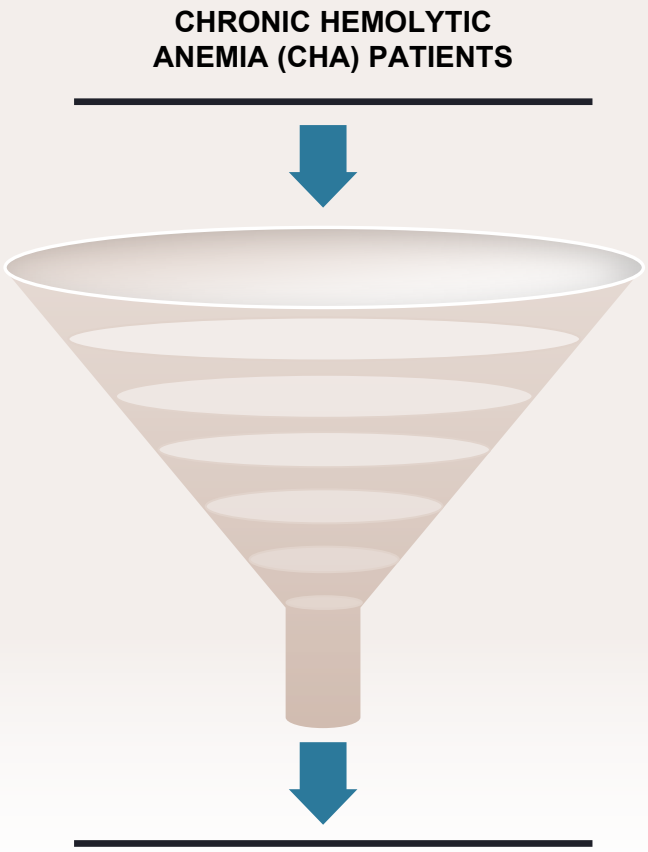
~25% of kits have been completed, and the PK deficiency positivity rate for completed tests remains in the mid-single digit percentages

Of the PK deficiency positive tests, they are **~40% pediatric and ~60% adult patients**

PYRUKYND® is not indicated for pediatric PK deficiency patients.

Lack of urgency defines the disease in terms of diagnosis and treatment

Goal to elevate PK deficiency testing in diagnostic triage



STEP

Key Drop Off

- Diagnose CHA
- Exclude Autoimmune Hemolytic Anemia
- Exclude Hemoglobinopathy

Key Drop Off

- Exclude Membranopathy
- PK Enzyme Test
- PKLR Genetic Test

Key commercial priorities based on learnings from launch

- Improve diagnostic urgency by highlighting the availability of PYRUKYND®
- Empower and activate patients to play a more active role in diagnosis and treatment
- Continue efficient HCP target identification

Source: Lab Director Interviews; Physician Interviews; ClearView Analysis. AIHA: Autoimmune Hemolytic Anemia; CHA: Chronic Hemolytic Anemia; PKD: Pyruvate Kinase Deficiency.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Third quarter 2022 financial results[1]

Statement of Operations	Three Months Ended 9/30/22	Three Months Ended 9/30/21
PYRUKYND® Net Revenue	$3.5M	--
Cost of Sales	$0.5M	--
Research & Development Expense	$65.0M	$64.0M
Selling, General & Administrative Expense	$29.1M	$27.2M
Royalty Income from Gain on Sale of Oncology Business (TIBSOVO® Royalties)	$4.4M	$2.0M

Balance Sheet	9/30/22	9/30/21
Cash, Cash Equivalents and Marketable Securities[2]	$1.0B	$1.4B

[1] Includes continuing operations on a comparative basis, which excludes results from divested oncology business.
[2]This cash position does not include the receipt of a one-time payment of $131.8 million associated with the sale of royalty rights on U.S. net sales of Servier's TIBSOVO®.

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Q&A

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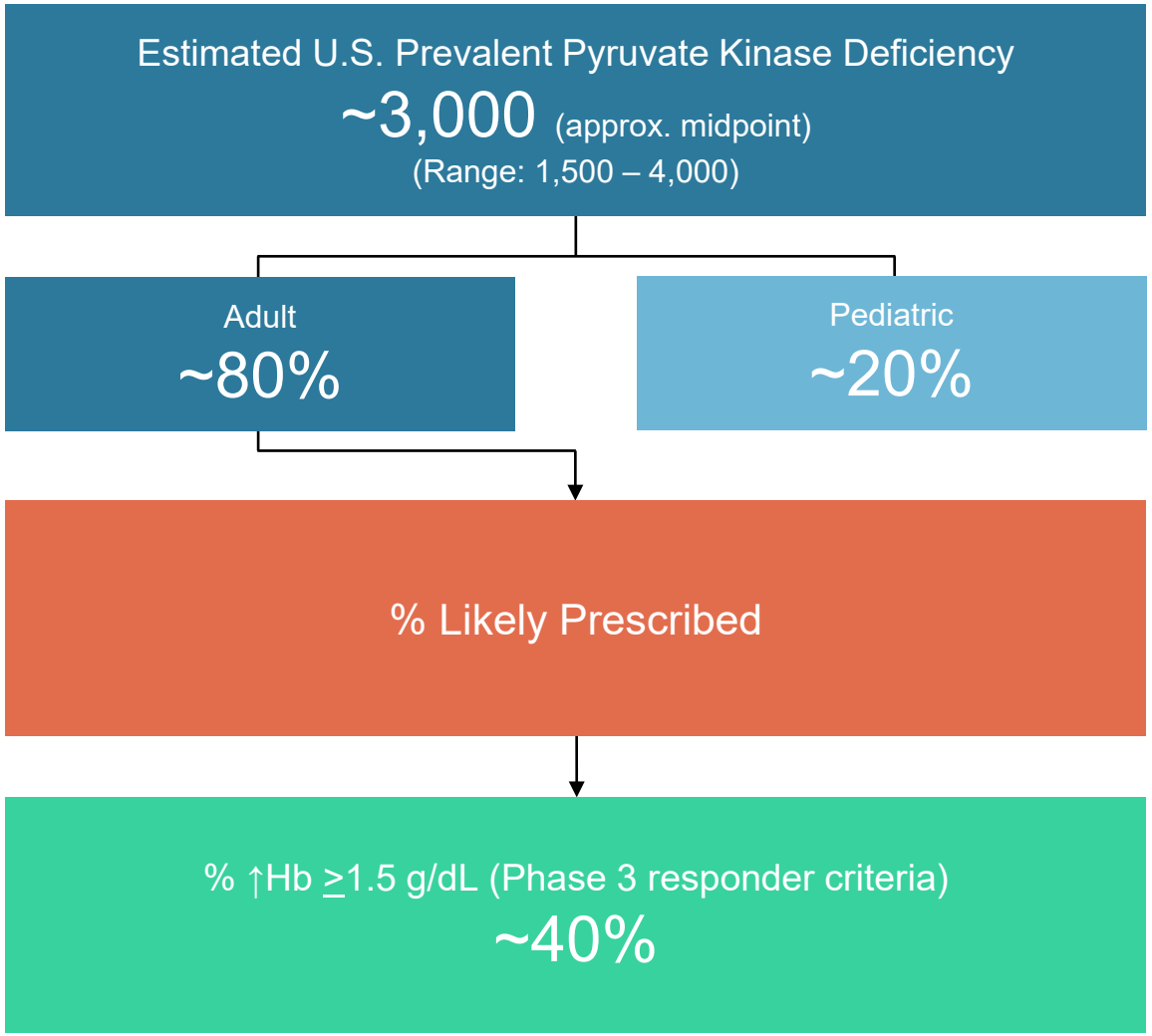
Appendix

Our understanding of the U.S. PK deficiency population for PYRUKYND® today



- Estimate ~30%+ diagnosed today
- Expect peak diagnosis to be in the 70-80% range, consistent with other rare diseases

Exclusions from Phase 3 studies:

- 30% patients have Hb ≥10 g/dL (Natural History Study)
- 9-15% double non-missense (Peak Registry)

- Expect eligible patients who initiate treatment to try for 6 months before clinical assessment of response based on label
- Payors may want to recertify patients at 3-6 months

- An additional 5% of patients likely to achieve improvement between 1.0 to 1.5 g/dL
- For responders, adherence likely to align to other chronic treatment

KEY DETAILS AND CONSIDERATIONS