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Q2 2022 Financial Results

August 4, 2022

Agios conference call participants

TOPIC	PARTICIPANT
Introductions	Holly Manning, Senior Director of Investor Relations
Business Update	Jackie Fouse, Ph.D., Chief Executive Officer
Clinical Development Update	Sarah Gheuens, M.D., Ph.D., Chief Medical Officer, Head of Research and Development
Commercial Update	Richa Poddar, Chief Commercial Officer
Second Quarter 2022 Financial Results	Jonathan Biller, Chief Financial Officer, Head of Corporate Affairs
Q&A	Dr. Fouse, Dr. Gheuens, Ms. Poddar, Mr. Biller

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 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; 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; 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 forward-looking 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.

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We are fueled by *connections.*

2022 AT-A-GLANCE

PYRUKYND FDA APPROVAL & U.S. LAUNCH
FEBRUARY

RESEARCH EVOLUTION
MAY

SIGNIFICANT PRESENCE AT EHA
JUNE

INITIATED PEDIATRIC PKD STUDIES
JUNE

CEO SUCCESSION ANNOUNCEMENT
JULY

Agios' Next CEO
Brian Goff

Experienced
in rare genetic diseases, hematology, commercial operations

Committed
to furthering our vision

Dedicated
to patients

Supported
by our leadership team & Board

Connected
to the Agios values & culture

Bold Decision Making

- Streamlined our portfolio
- Evolved our strategic focus
- Shifted our research approach

Operating from a position of strength to deliver *value for all stakeholders*

- First-in-class commercial launch
- 5 pivotal trials underway
- Multiple early-stage studies planned or underway
- Promising preclinical pipeline
- Enviable balance sheet


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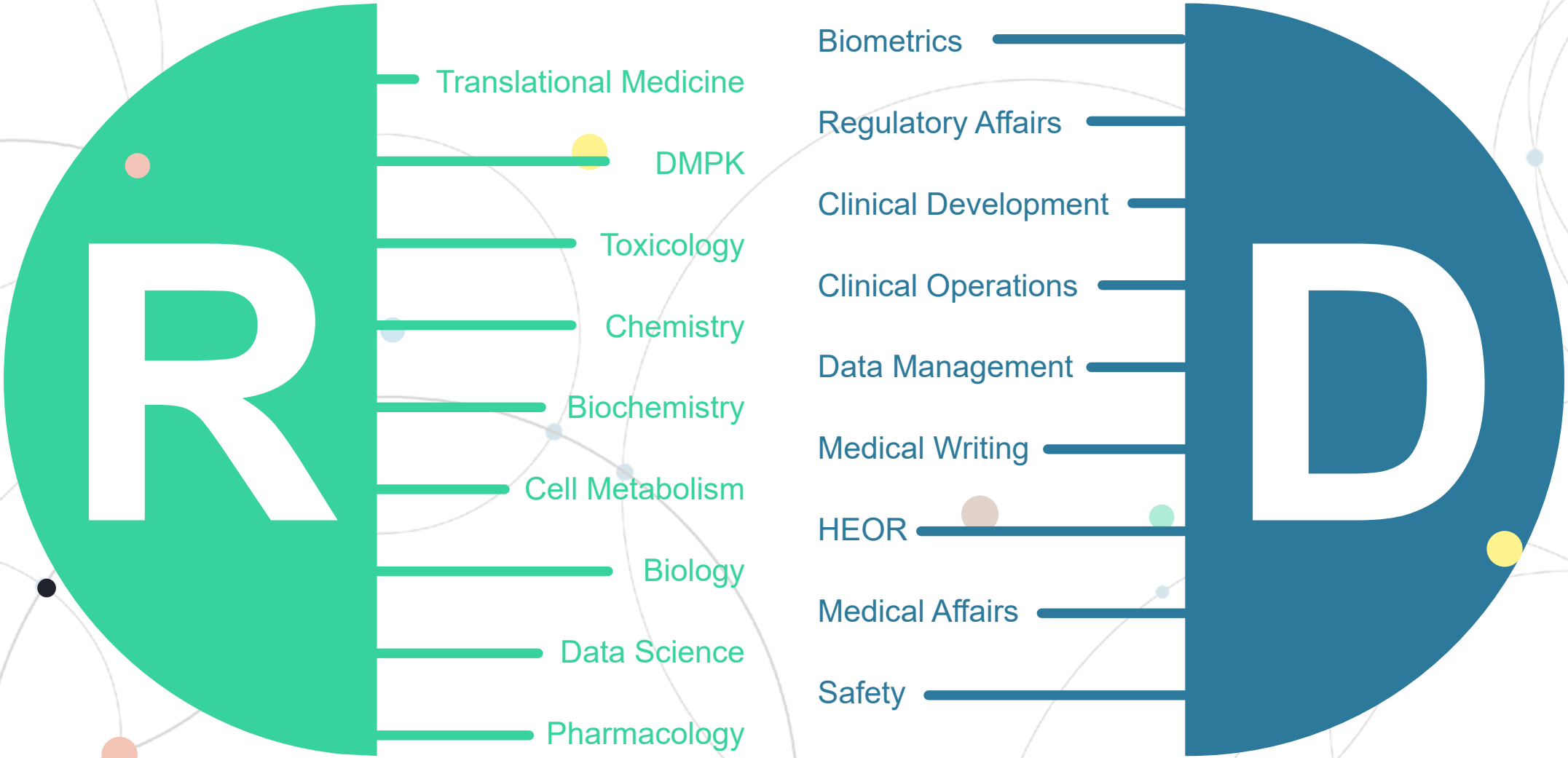
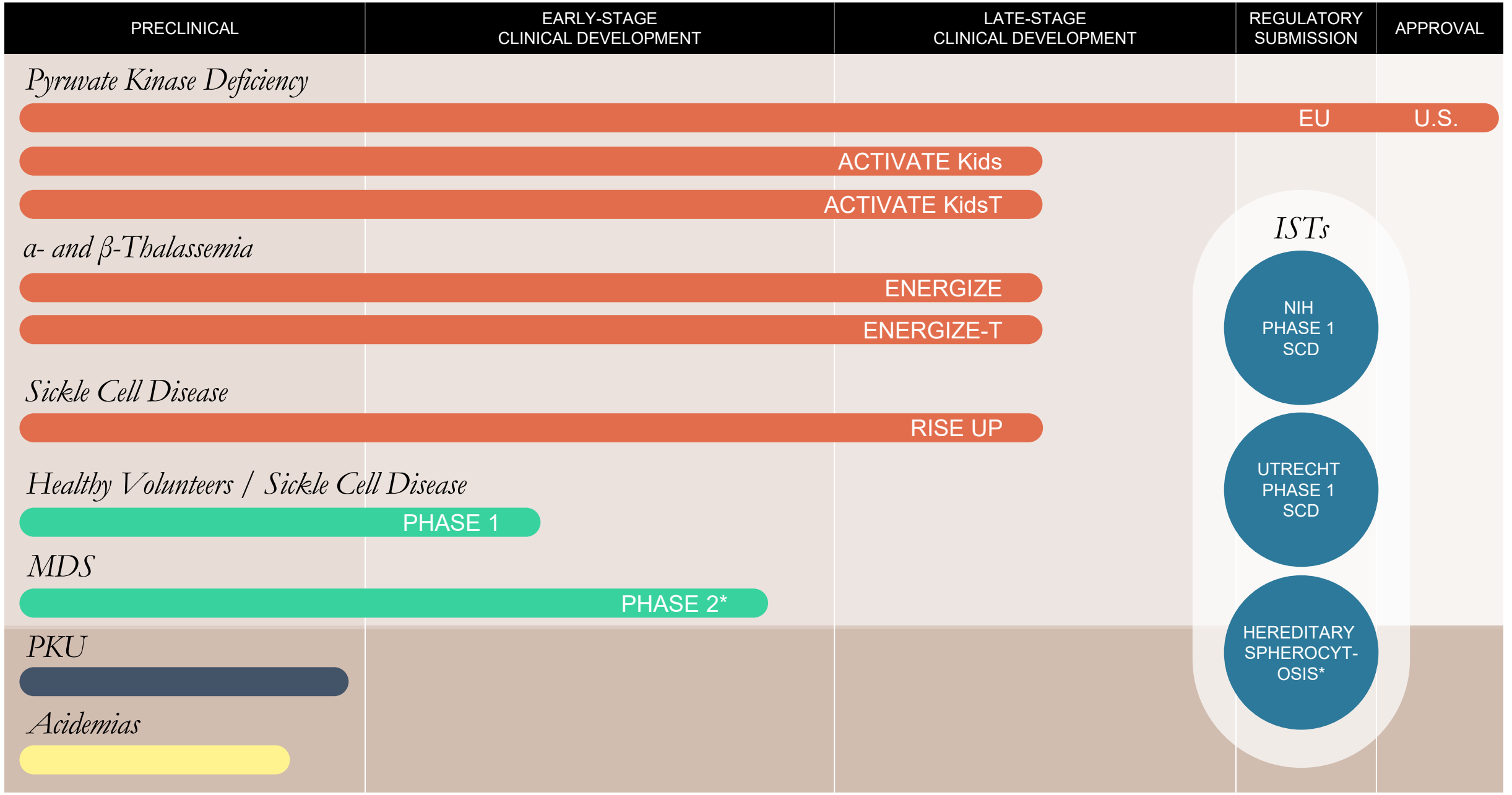
One Research & Development Team



HEOR = health economics and outcomes research; DMPK = drug metabolism and pharmacokinetics



PYRUKYND® AG-946 PAH BCAT2

*Near-term initiation expected

Promising preclinical pipeline: Branched chain amino acid aminotransferase-2 (BCAT2) inhibitors for the treatment of propionic (PA) and methylmalonic (MMA) acidemia

ACUTE METABOLIC DECOMPENSATION → **CHRONIC MANIFESTATIONS**

- Occurs shortly after birth if untreated
- Triggered by external factors later in life
- Can be fatal and produce long-lasting damages

- Delayed/reduced cognitive development
- Renal insufficiency (MMA) / cardiac issues (PA)

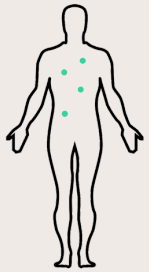
MMA and PA are associated with increased mortality (few patients over 35)

- PA and MMA are a group of inherited in-born errors of metabolism, in which the body cannot break down branched chain amino acids, leading to a toxic accumulation
- ~5-10K PA and MMA patients in the U.S./EU
- PA and MMA are currently managed by restrictive diet and supplements, however current approaches are insufficient
- BCAT2 inhibition has the potential to reduce the formation of the toxic metabolites, methylmalonic acid and propionic acid
- Prevention of this accumulation may lead to a decrease in metabolic crises, enabling patients to have fewer dietary/other restrictions and improved quality of life

 Source: Agios internal estimates

Promising preclinical pipeline: Phenylalanine hydroxylate (PAH) stabilizers for the treatment of phenylketonuria (PKU)

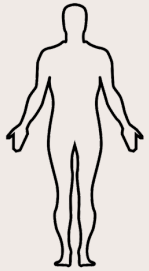
1



Normal Protein Diet

A mixed diet provides your body Phe

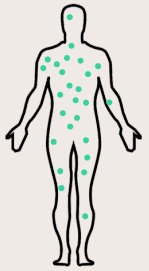
2



Defective PAH enzyme

PAH fails to process the Phe to Tyr

3

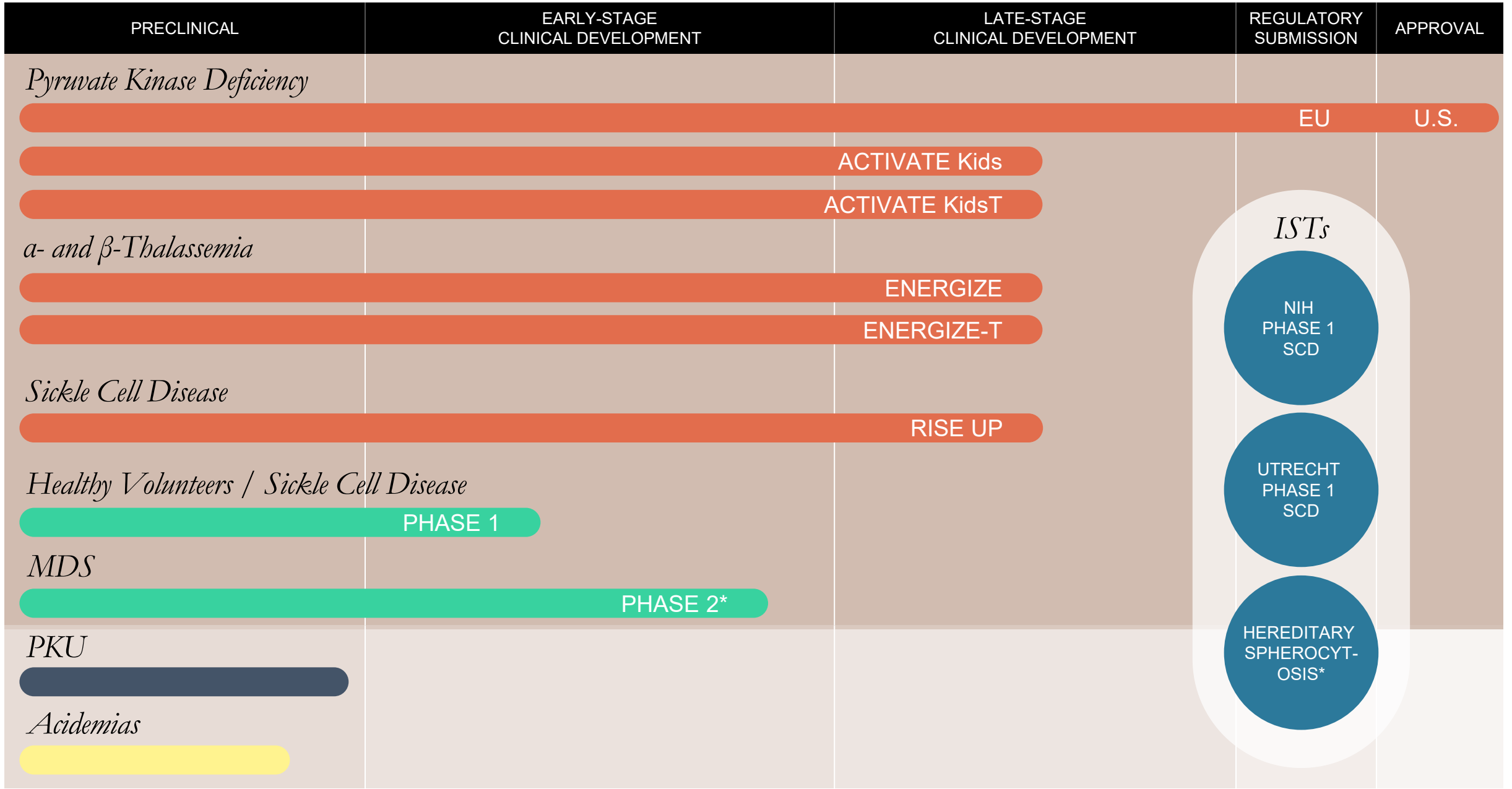


Increase in Phenylalanine

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

- PKU is a rare, inherited disease that causes phenylalanine to accumulate, which leads to neurocognitive defects and intellectual disability
- ~15-20K PKU patients in the U.S.; ~20K in the EU5
- Highly restricted diet is key part of the standard of care, thus a high unmet medical need remains
- Normalizing plasma phenylalanine concentrations with a PAH stabilizer may allow patients to increase natural protein intake and provide them with increased quality of life
- Program is approaching the development candidate milestone, and we expect to achieve an IND in 2023

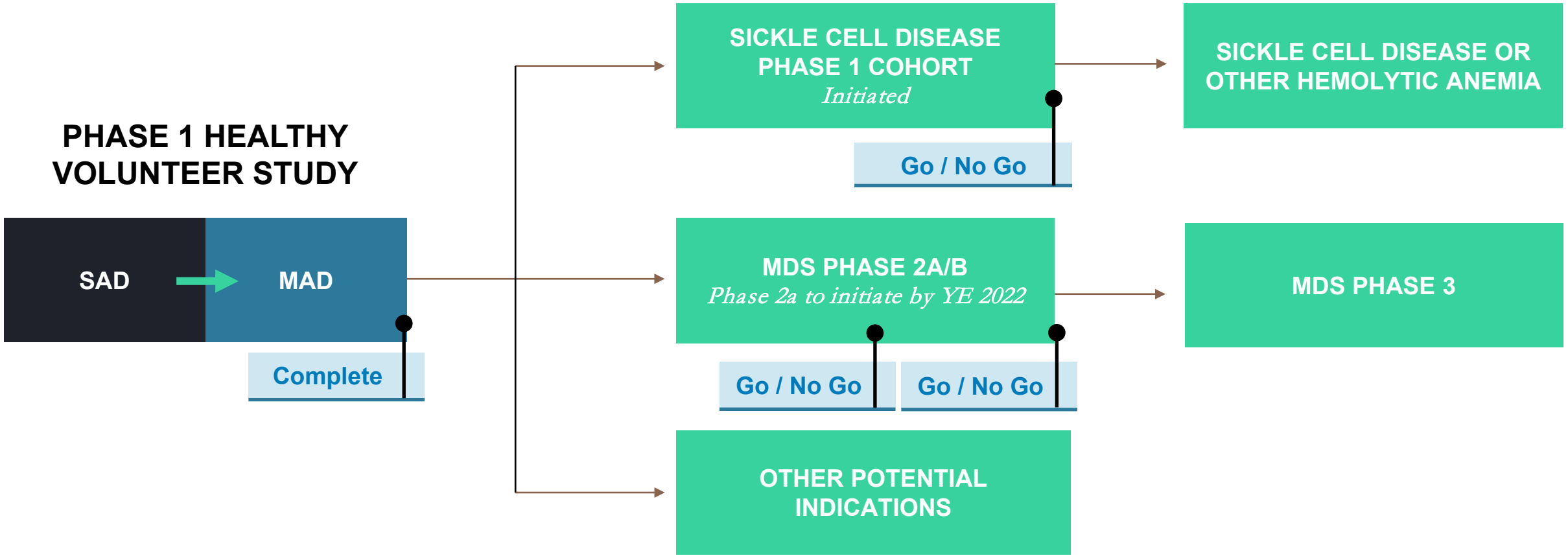
Sources: National PKU Alliance, www.npkua.org and Weisbren et al 'Phenylalanine blood levels and clinical outcomes in phenylketonuria'; The American Journal of Human Genetics 107, 234–250, August 6, 2020; Agios internal estimates



PYRUKYND® AG-946 PAH BCAT2

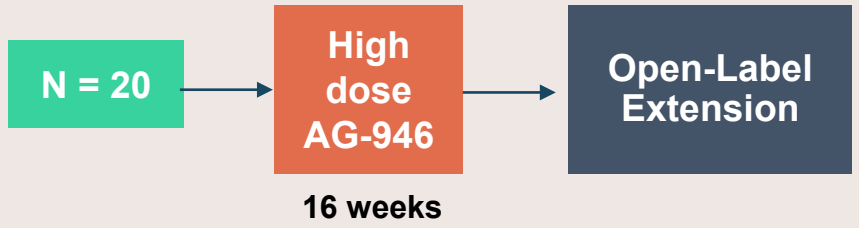
*Near-term initiation expected

AG-946 clinical development plan: Ability to pursue multiple paths in parallel if data support advancement



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

Phase 2a — Open Label

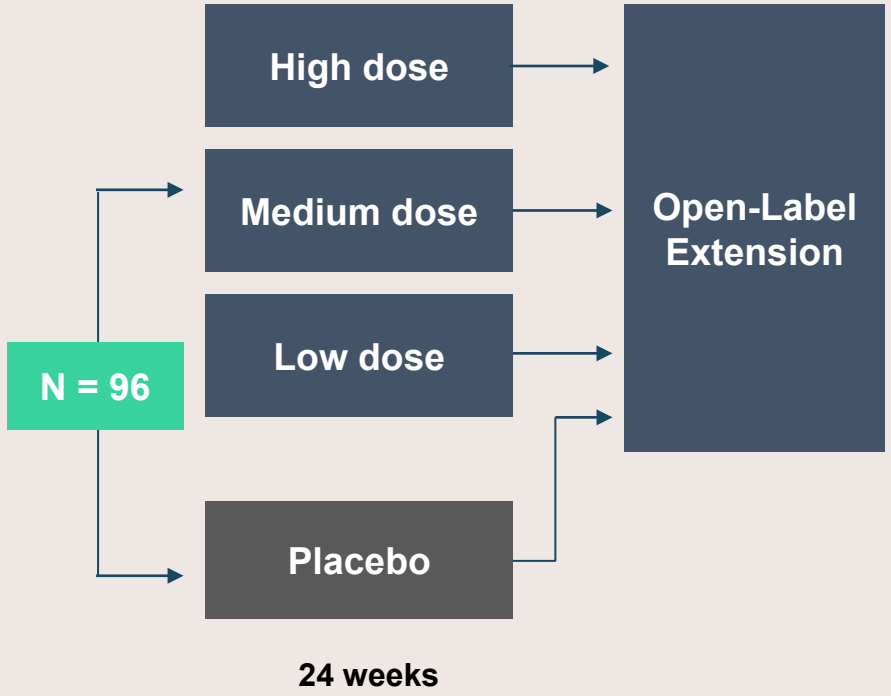


Primary endpoints:

- 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



Our clinical focus for PYRUKYND® is to transform the course of hemolytic anemia by increasing RBC *energy, health and longevity* to address commonality in pathophysiology and unmet need across PK deficiency, thalassemia and SCD

In PK deficiency, thalassemia and sickle cell disease, RBCs have:

- Insufficient energy
- Increased oxygen radical injury
- Abnormal RBC shape changes

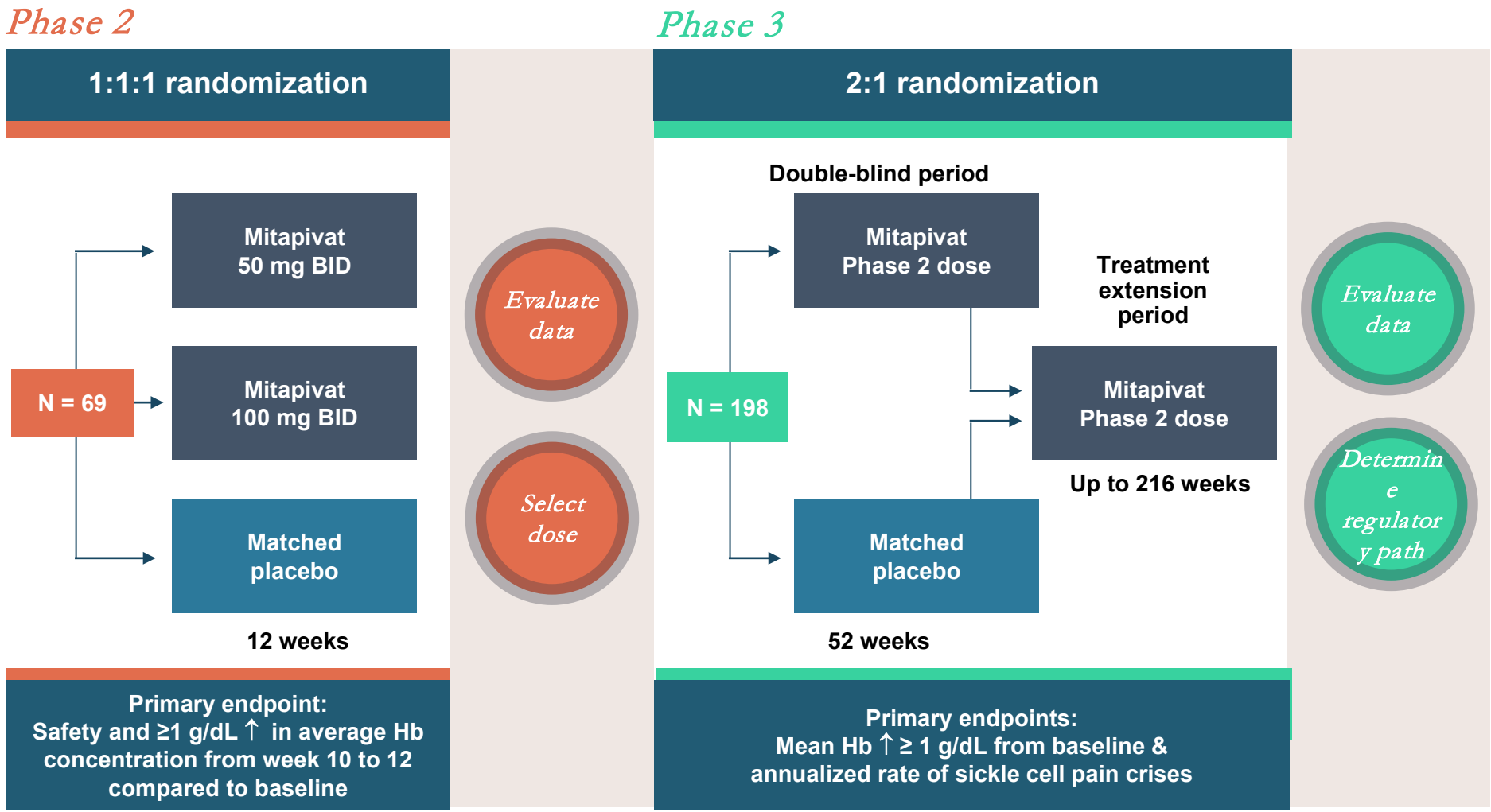
All of these hemolytic anemias cause major complications and impact patient quality of life

- Chronic fatigue, iron overload
- Challenges with social, emotional health
- Challenges with school and work activities
- Potentially serious complications

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

ENROLLMENT CRITERIA

- ≥ 16 years
- Had 2-10 sickle cell crises in the past 12 months
- Hb ≥ 5.5 and ≤ 10.5 g/dL
- Patients currently receiving treatment with voxelotor, crizanlizumab, or any other agent intended to increase Hb-oxygen affinity are excluded
- Treatment with hydroxyurea is allowed



BID = twice daily; Hb = hemoglobin

Expect to complete enrollment in the Phase 2 portion by YE

ENROLLMENT CRITERIA

- ≥ 16 years
- Had 2-10 sickle cell crises in the past 12 months
- Hb ≥ 5.5 and ≤ 10.5 g/dL
- Patients currently receiving treatment with voxelotor, crizanlizumab, or any other agent intended to increase Hb-oxygen affinity are excluded
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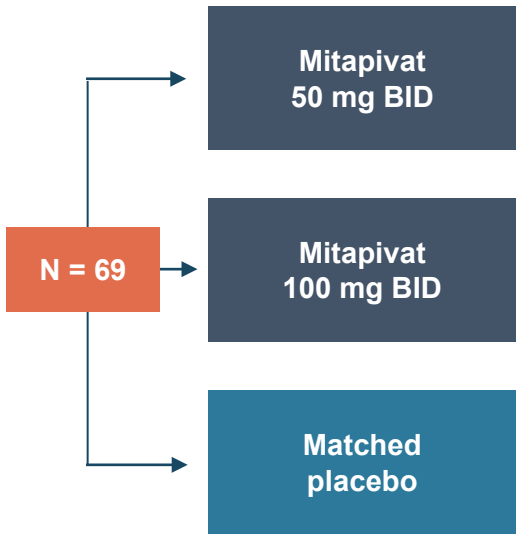
Phase 2

1:1:1 randomization



12 weeks

Primary endpoint:
Safety and ≥1 g/dL ↑ in average Hb concentration from week 10 to 12 compared to baseline

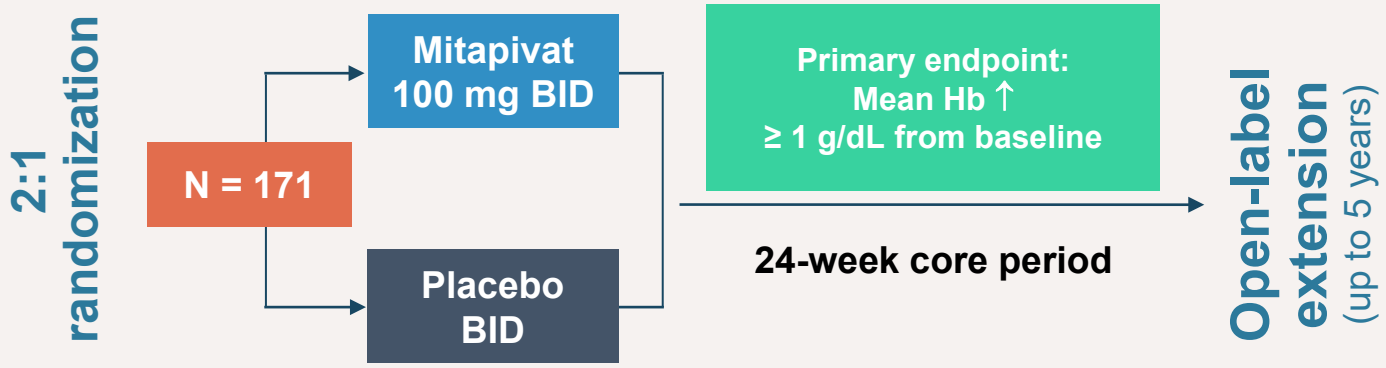
Evaluate totality of data to trigger Phase 3 including:

- Hemoglobin response
- Safety profile
- Change in markers of hemolysis
- Rate of sickle cell pain crises
- Patient reported fatigue
- Other secondary endpoints

BID = twice daily; Hb = hemoglobin

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

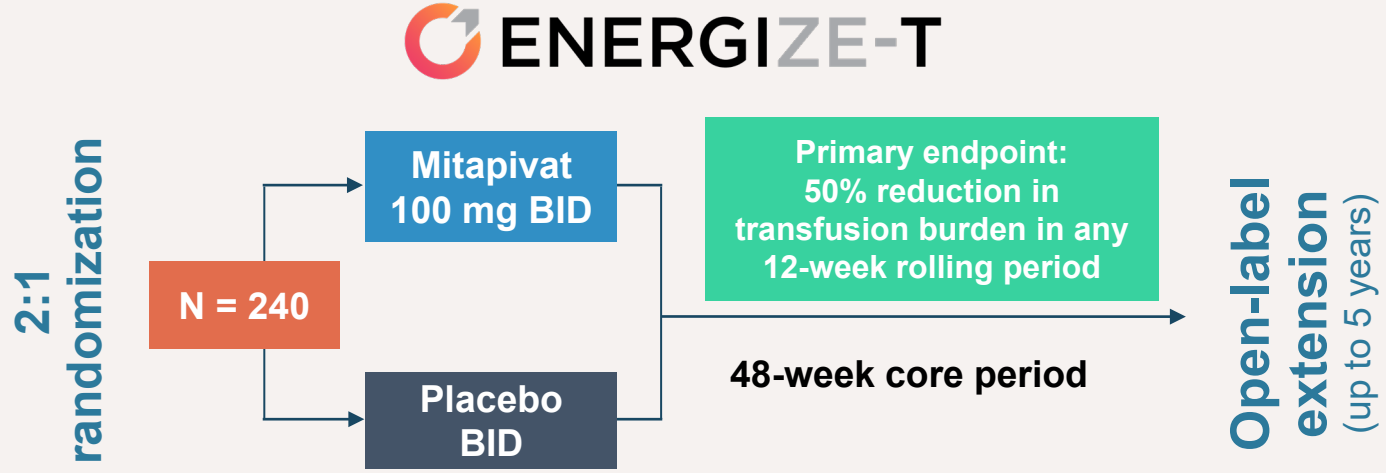
ENERGIZE



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



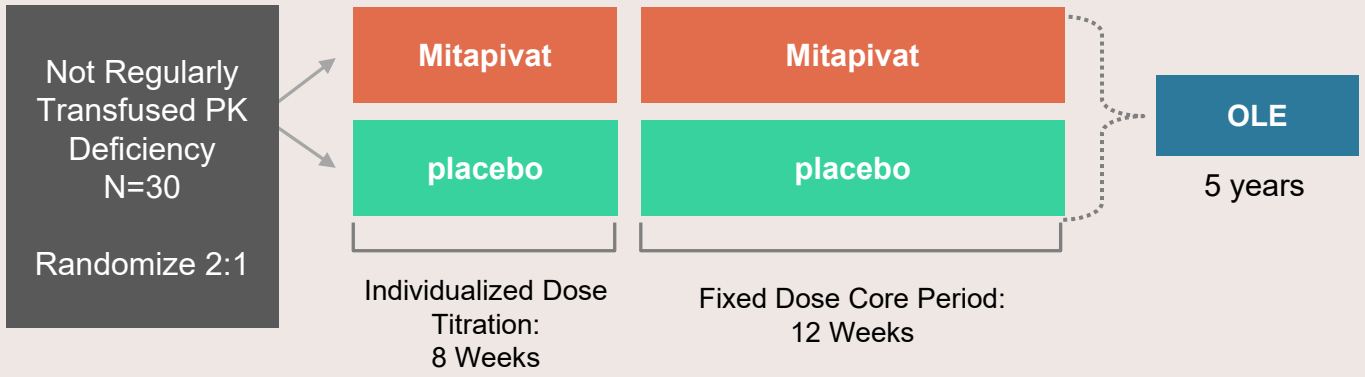
Key inclusion criteria

- ≥ 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.

ACTIVATE-Kids and ACTIVATE-KidsT, Agios' first pediatric clinical program in PK deficiency, open and enrolling patients

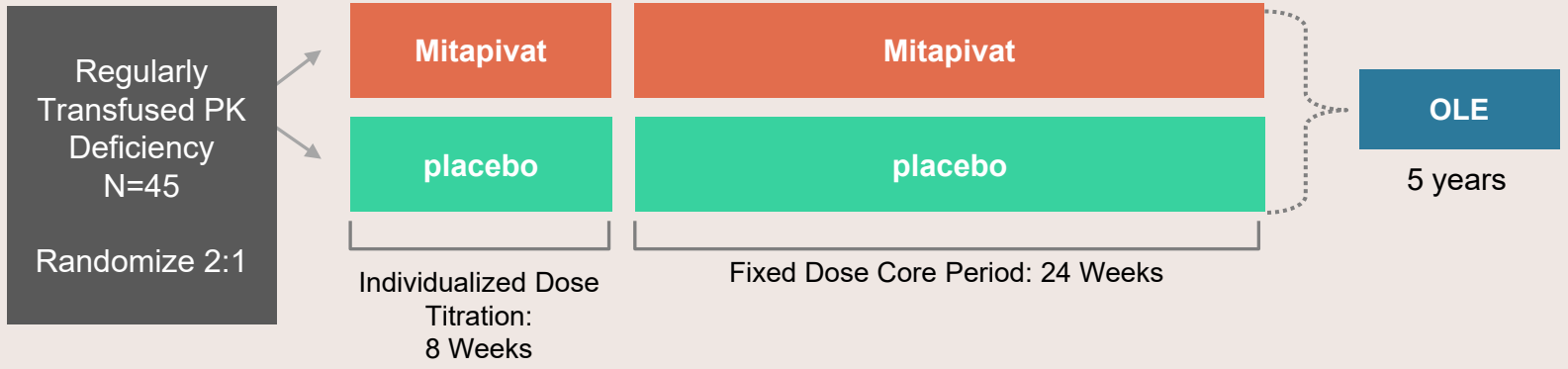
ACTIVATE-Kids™



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

Significant progress against anticipated 2022 key milestones & priorities

FDA approval and launch of mitapivat in adults with PK deficiency

Initiate two Phase 3 studies of mitapivat in pediatric patients with PK deficiency

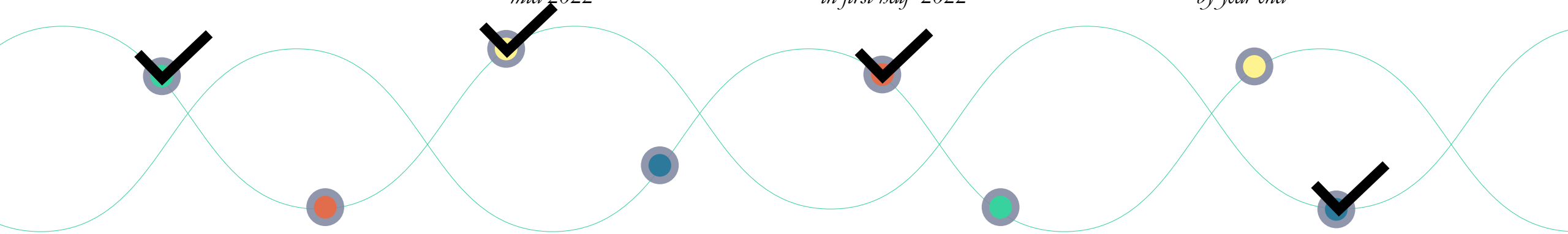
mid-2022

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

in first half 2022

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

by year-end



Potential EMA approval of mitapivat in adults with PK deficiency

by year-end

Complete enrollment in the Phase 2 portion of the RISE UP study of mitapivat in adults with SCD

by year-end

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

by year-end

Continue to publish 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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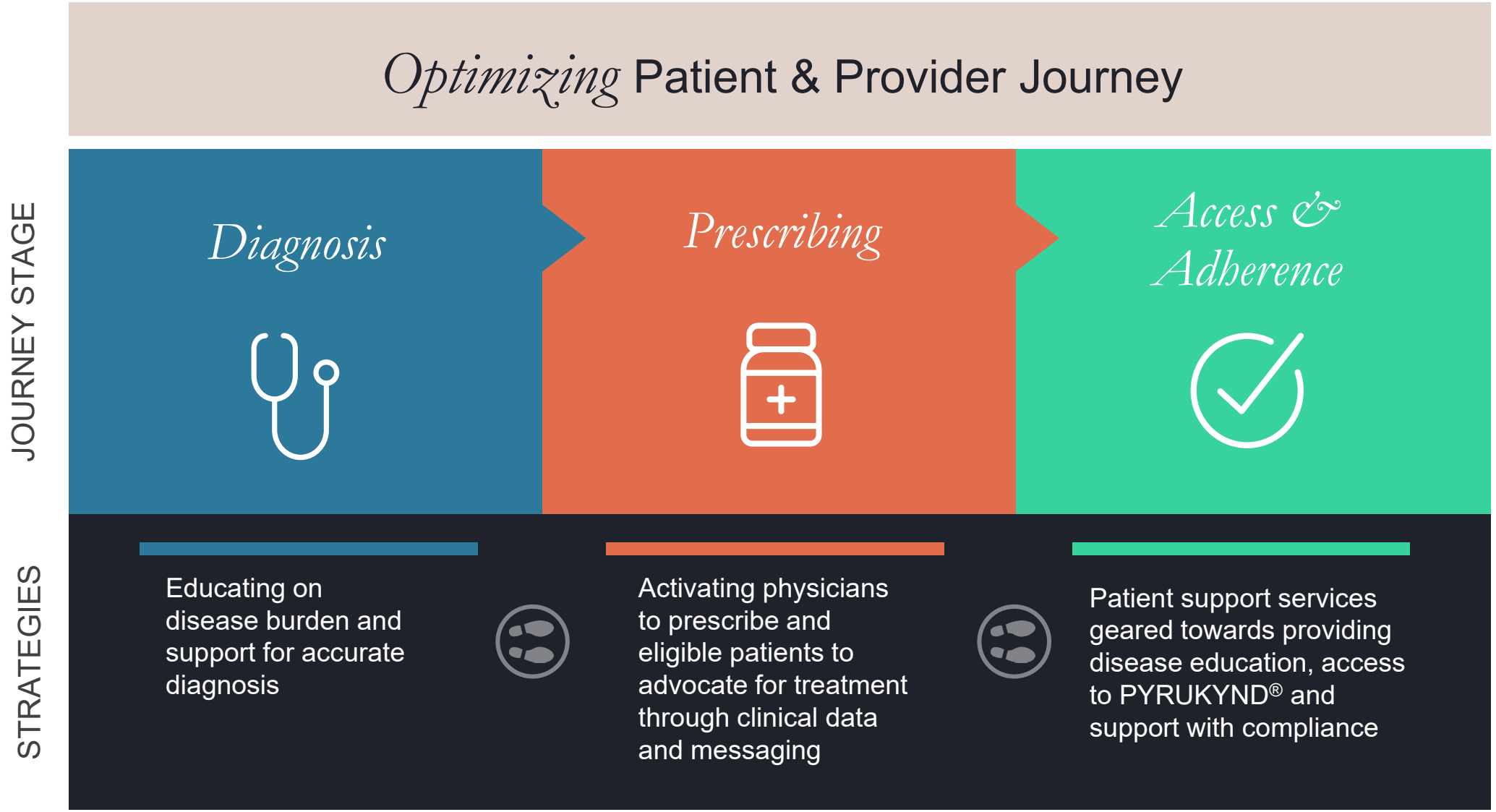
Comprehensive commercial strategy informed by deep understanding of the PK deficiency patient journey & focused on delivering launch success



PYRUKYND® Q2 2022 performance metrics highlight early launch health

$3.1M net U.S. sales of PYRUKYND®
for first full quarter of launch

52 unique patients completed PYRUKYND® prescription enrollment forms

37 patients on PYRUKYND®, which includes new prescriptions and those continuing treatment and represents a range of demographics and disease characteristics

Unique prescriber base of 50 physicians, diversified across the country

Continued positive interactions with payors; prior authorization and utilization management criteria are being developed

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

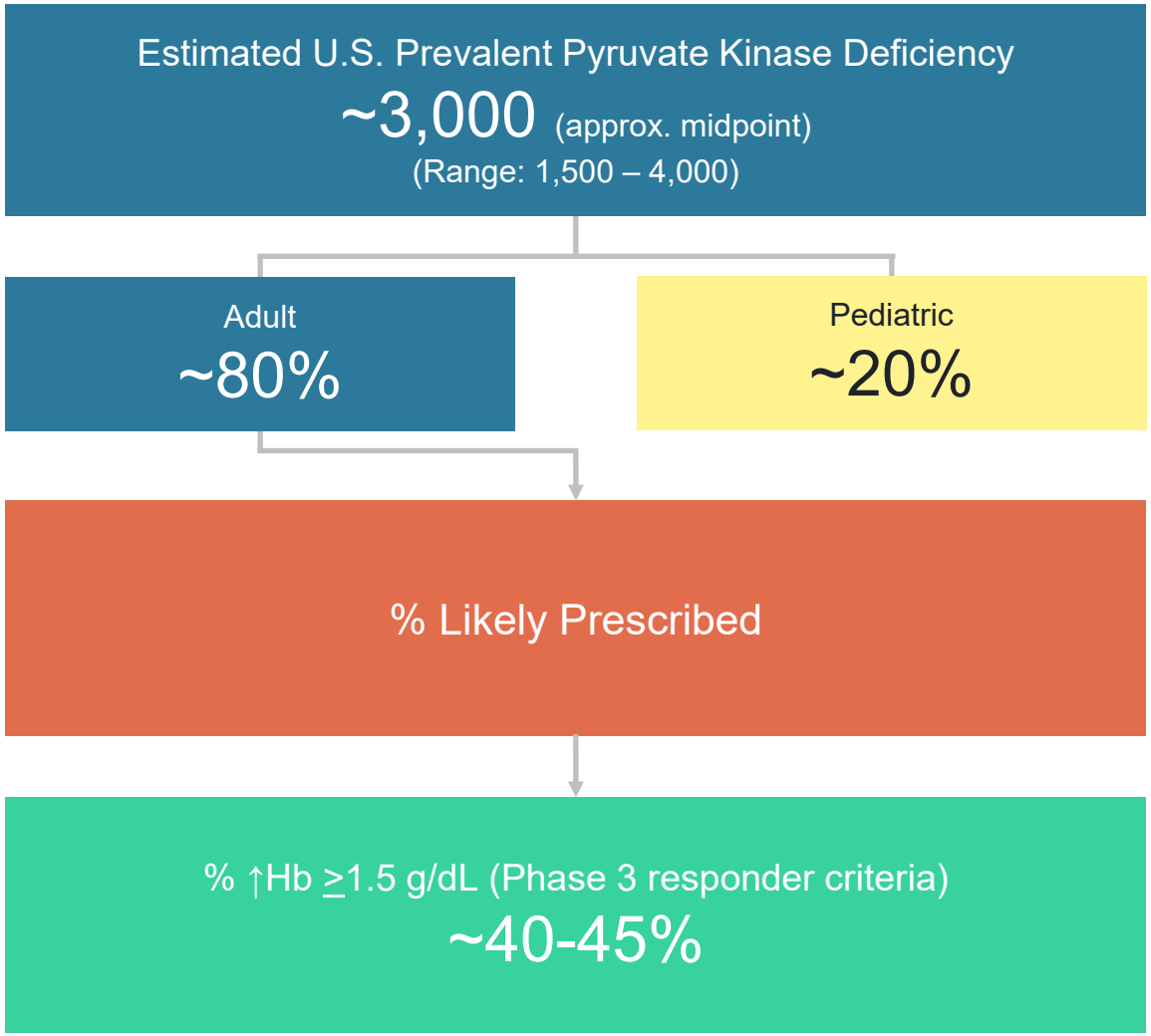
As of June 30:

More than 4,200 kits have been ordered, a 20% increase since Q1

~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 *split evenly between pediatric and adult patients*

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:

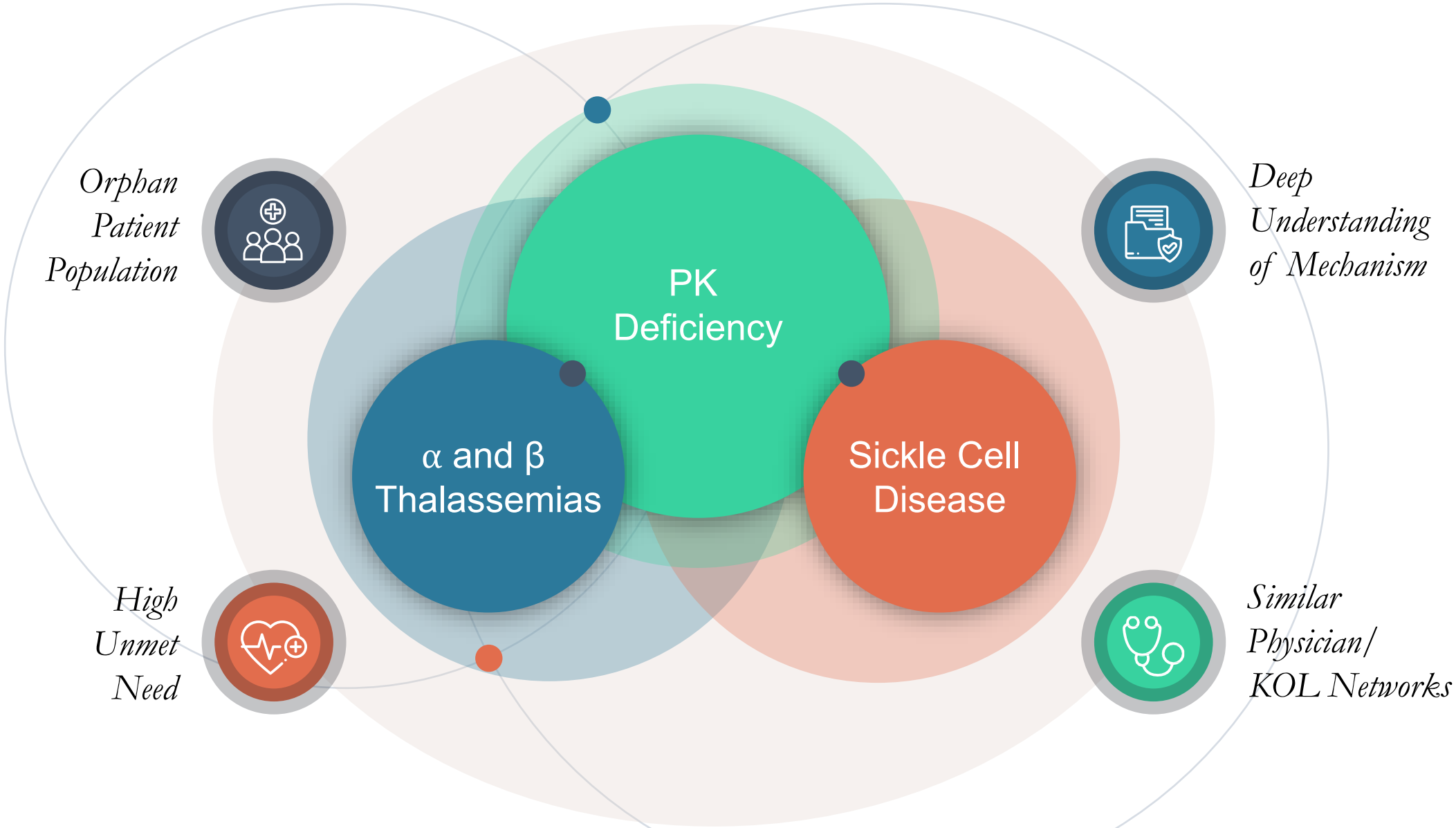
- 30% patients have Hb ≥10 g/dL (Natural History Study)
- 9-15% double non-missense (Peak Registry)

- 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
- Consider likely adherence to chronic treatment

Key Details and Considerations

Broad scientific and commercial experience with PK deficiency positions Agios well for potential expansion to thalassemias and SCD

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Second quarter 2022 financial results[1]

Statement of Operations	Three Months Ended 6/30/22	Three Months Ended 6/30/21
PYRUKYND® Revenue	$3.1M	--
Other Revenue[2]	$2.5M	--
Cost of Sales	$0.4M	--
Research & Development Expense	$74.5M	$62.0M
Selling, General & Administrative Expense	$28.3M	$29.2M
Royalty Income from Gain on Sale of Oncology Business (TIBSOVO® Royalties)	$2.7M	$2.0M

Balance Sheet	6/30/22	6/30/21
Cash, Cash Equivalents and Marketable Securities	$1.1B	$1.7B

[1] Includes continuing operations on a comparative basis, which excludes results from divested oncology business.
[2] Recognized revenue of $2.5 million dollars due to an up-front payment associated with the licensing of intellectual property for the Friedreich's Ataxia preclinical program.

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Q&A