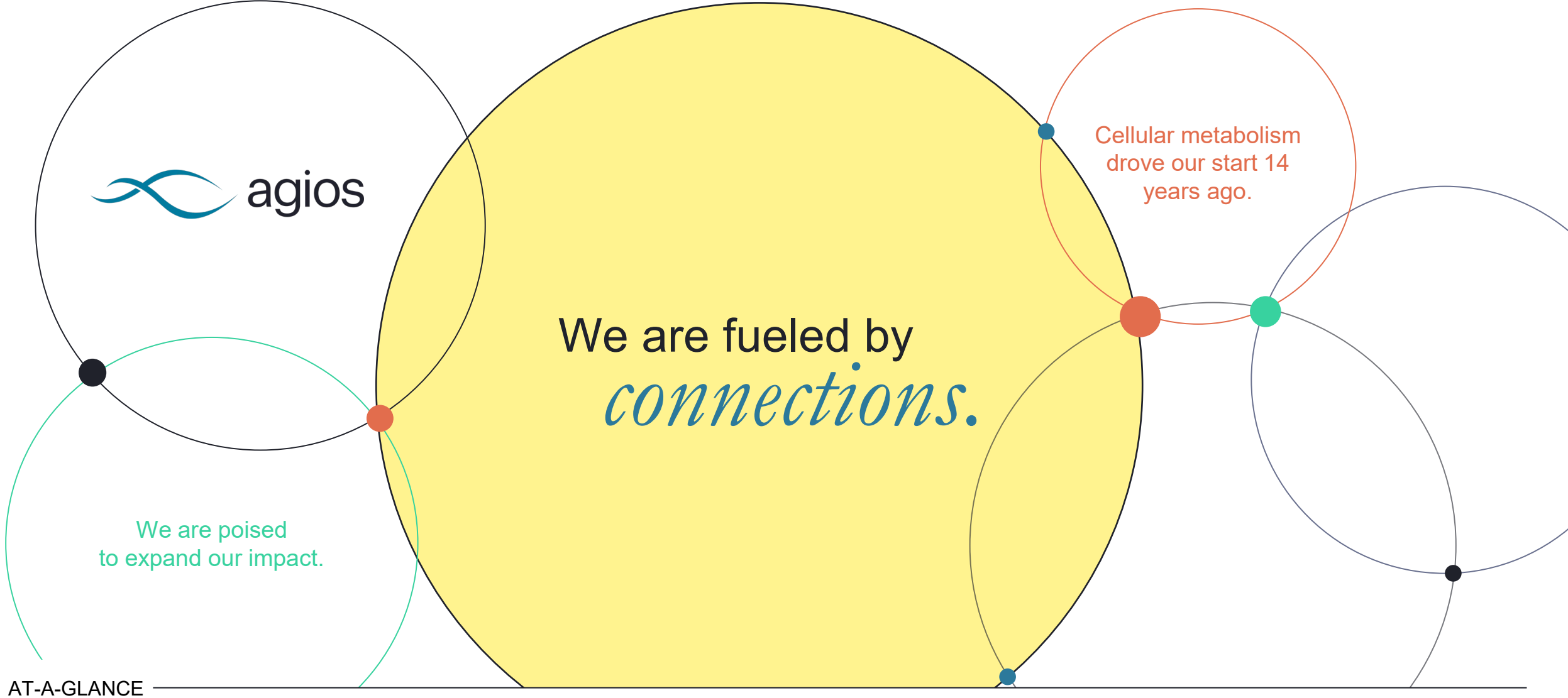
agios

PYRUKYND® (mitapivat) FDA Approval

February 18, 2022

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) and AG-946; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND® and AG-946; Agios' key milestones for 2022; Agios' plans regarding future data presentations; 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; 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.



AT-A-GLANCE

FOUNDED
2008

IPO
July 2013

1ST APPROVED THERAPIES
2017 & 2018

1ST GENETICALLY DEFINED DISEASE APPROVAL
2022

HEADQUARTERS
Cambridge, Mass.

Strong connections to patients mean we *listen* to and work *with* them to create solutions

Kim
Pyruvate Kinase Deficiency

Ryan
Thalassemia

Sharonda
Sickle Cell Disease

We are the pioneering leaders in PK activation

PIVOTAL CLINICAL PROGRAMS

- ACTIVATE
- ACTIVATE-T
- ENERGIZE
- ENERGIZE-T
- RISE UP

PUBLICATIONS

DISEASES WITH POC ACHIEVED

- PK Deficiency
- Thalassemia
- Sickle Cell Disease

+ A LOT OF FIRSTS:

- 1st GLOBAL PK DEFICIENCY REGISTRY
- 1st INTERNATIONAL PK DEFICIENCY ADVOCACY COUNCIL
- 1st HEMOLYTIC ANEMIA ADVOCACY COALITION BUILDING
- 1st CLINICAL TRIAL EVALUATING TREATMENT IN α-THALASSEMIA
- 1st APPROVED THERAPY FOR PK DEFICIENCY

Now approved

pyrukynd®
(mitapivat) tablets

PYRUKYND® U.S. Prescribing Information Overview

PYRUKYND® USPI highlights*

Indications & Usage

- PYRUKYND® is a pyruvate kinase activator indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency.

Dosage & Administration

- The starting dosage for PYRUKYND® is 5 mg orally twice daily. PYRUKYND® is taken with or without food and swallowed whole. Do not split, crush, chew, or dissolve the tablets.
- To gradually increase hemoglobin (Hb) levels, titrate PYRUKYND® from 5 mg twice daily to 20 mg twice daily, and then to the maximum recommended dose of 50 mg twice daily, with these dose increases occurring every 4 weeks
- Discontinue PYRUKYND® if no benefit has been observed by 24 weeks, based on the hemoglobin and hemolysis laboratory results and transfusion requirements.

Warnings & Precautions

- Acute Hemolysis: Avoid abrupt interruption or abrupt discontinuation of PYRUKYND® to minimize the risk of acute hemolysis. A gradual reduction in dosing rather than abrupt cessation is recommended when possible.

* The full prescribing information can be found on our website at agios.com.

PYRUKYND® USPI highlights* (continued)

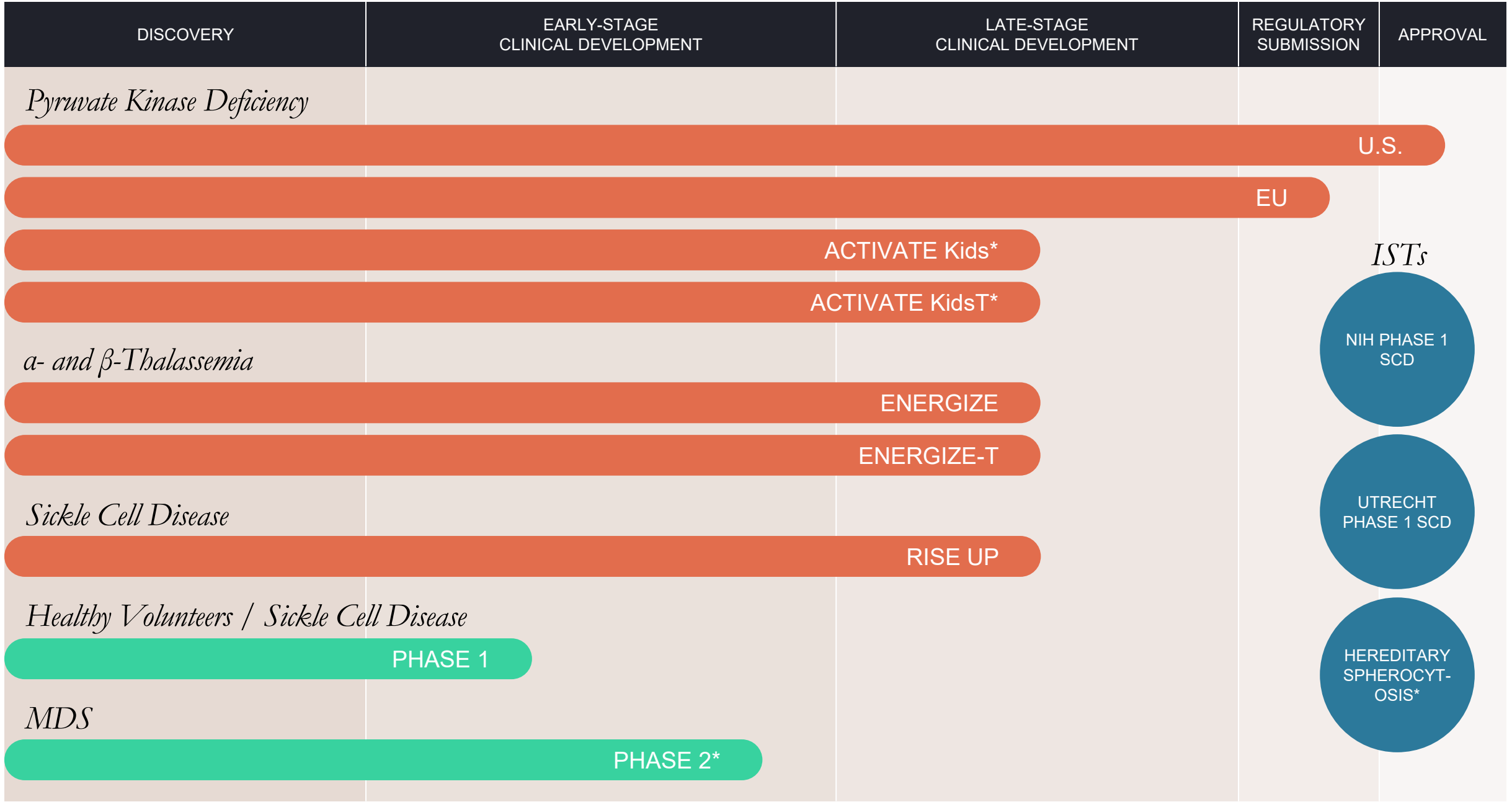
ACTIVATE Data

- 40% of patients achieved an Hb response[1] in the PYRUKYND® arm compared to 0% in the placebo arm.
- Treatment with PYRUKYND® also demonstrated statistically significant improvements over placebo across pre-specified secondary endpoints including markers of hemolysis and ineffective erythropoiesis.
- The LS Mean change from baseline with PYRUKYND compared to placebo was -0.4 (standard error [SE] 0.1) for jaundice (scale: 0-4), -1.1 (SE 0.4) for tiredness (scale: 0-10), and -0.3 (SE 0.3) for shortness of breath (scale: 0-10), assessed with the daily Pyruvate Kinase Deficiency Diary (PKDD) where lower scores represent less sign/symptom severity.
- Serious adverse reactions occurred in 10% of patients receiving PYRUKYND®. Serious adverse reactions included atrial fibrillation, gastroenteritis, rib fracture, and musculoskeletal pain, which each occurred in 1 patient.
- The most common adverse reactions including laboratory abnormalities (≥ 10%) in patients with PK deficiency were estrone decreased (males), increased urate, back pain, estradiol decreased (males), and arthralgia.

ACTIVATE-T Data

- 33% of patients treated with PYRUKYND® achieved a transfusion reduction response.[2]
- 22% of patients treated with mitapivat were transfusion-free during the 24-week fixed-dose period.
- The adverse reactions reported in patients who were regularly transfused (ACTIVATE-T) were consistent with that seen in ACTIVATE.

* The full prescribing information can be found on our website at agios.com.
[1]Hb response was defined as ≥1.5 g/dL increase in Hb concentration from baseline sustained at 2 or more scheduled assessments (Weeks 16, 20, and 24) during the fixed dose period.
[2]Transfusion reduction response (TRR) and was defined as ≥33% reduction in the number of red blood cell (RBC) units transfused during the fixed dose period compared with the historical transfusion burden.

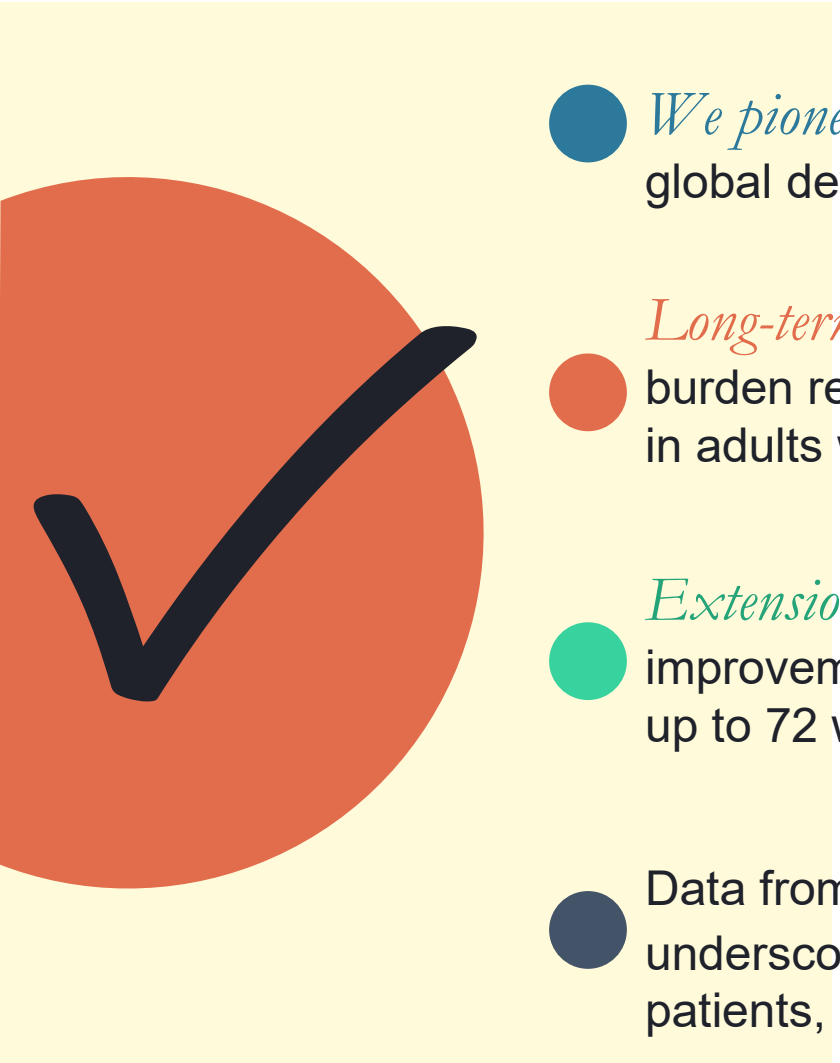


PYRUKYND®

AG-946

*Near-term initiation expected

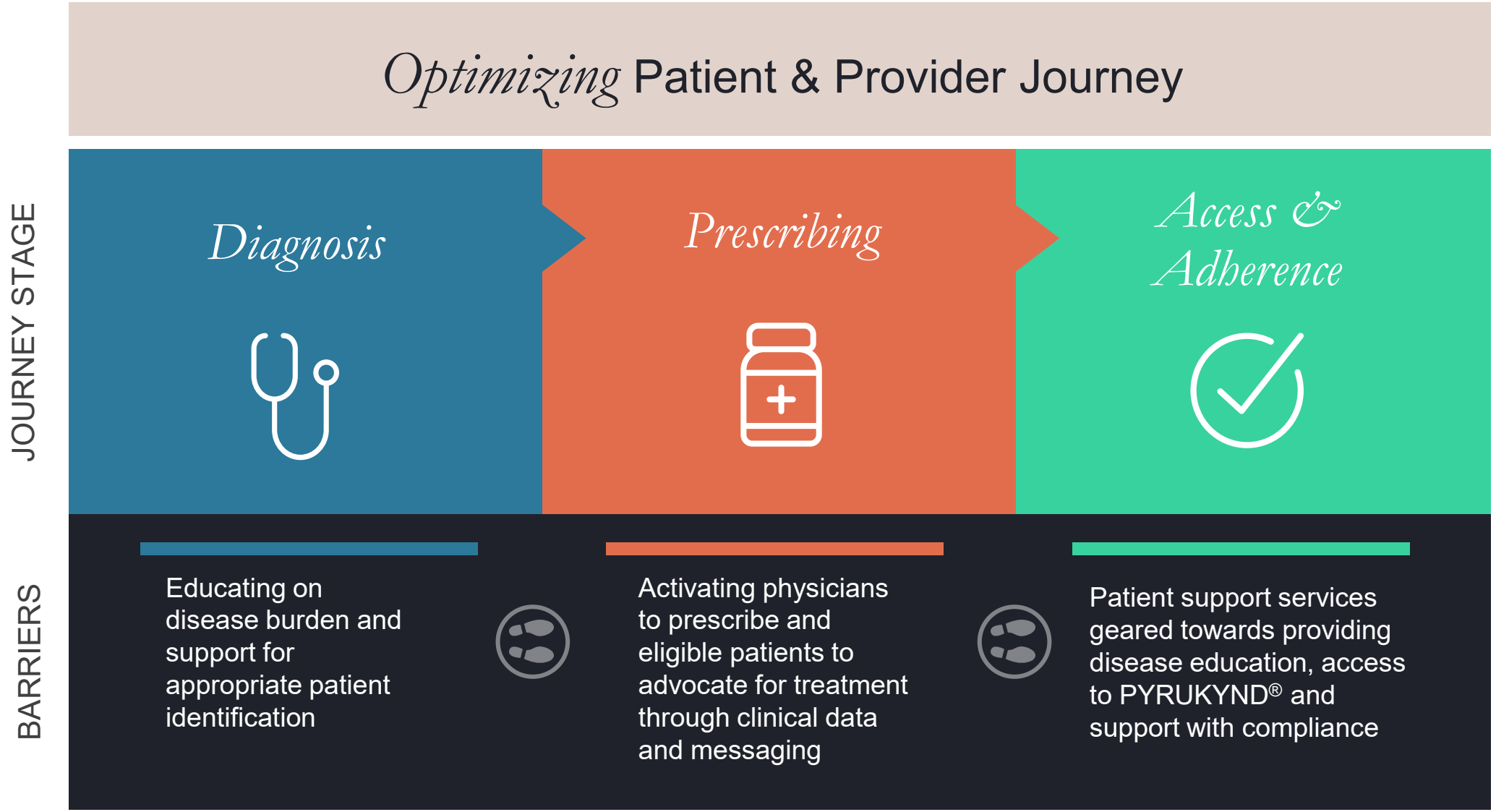
Our 7+ years of clinical experience with PYRUKYND® continues to validate the potential of PK activation across therapeutic areas



- *We pioneered* PK activation clinical development with a differentiated approach to global development and community partnerships
- *Long-term extension data* show durability of hemoglobin response, transfusion burden reduction, and improvement in ineffective erythropoiesis and iron overload in adults with PK deficiency
- *Extension data* for PYRUKYND® highlight long-term safety profile and durable improvement in hemoglobin and markers of hemolysis in thalassemia patients for up to 72 weeks
- Data from *investigator-led studies* of PYRUKYND® in adults with sickle cell disease underscore potential of mitapivat to improve clinically meaningful outcomes for patients, including anemia, hemolysis and sickling parameters

PYRUKYND® Commercial Launch

Commercial strategy to inform launch success



Exhaustive multi-channel approach to continuously improve diagnosis and disease understanding in PK deficiency

PK Deficiency Should Be Accurately Diagnosed to Ensure Appropriate Patient Care

Identify PK deficiency

- Claims-based Targeting
- Partnership with 23andMe
- Exploring Electronic Medical Records + ICD-10 codes
- Provider Customer Engagement

To date, 2-3K HCP targets profiled, each with average 3-5 hemolytic anemia patients

Activate providers and patient to obtain or confirm diagnosis

- AnemiaID offers free genetic testing on behalf of patients
- InformedDNA Genetics, Decoded. — Genetic counseling support to allow for patient-initiated testing

HCPs indicate they intend to order AnemiaID for ~85% of appropriate patients

Drive awareness and urgency to manage PK deficiency

- myagios™ — Empowers patients to proactively manage their disease
- Know PK Deficiency — Disease education campaign

Increasing awareness of HCPs around PK deficiency

Sources: Mitapivat PK Deficiency US Demand Study, Agios Commercial Analytics, Charles River Associates, June 2021, Agios Commercial Analytics, Oct 2021

Educating physicians and patients on PYRUKYND®

Guiding principles help inform our decisions and thinking related to access and pricing

Create meaningful outcomes for patients

We work tirelessly to understand genetically defined diseases, so we can develop medicines that help address the outcomes that are most important to people living with these diseases.

Stay connected with communities

We connect directly with patients, caregivers, advocates, providers, payers, and policymakers and are invested in collaborating with them to develop new and better solutions.

Emphasize transparency

We connect communities with the information they need by sharing our data, values, processes, and progress as openly as possible.

Ensure sustainability to help more patients

We invest in innovation to help more patient communities, while ensuring we continue to serve the patients of today.

The average annual wholesale acquisition cost (WAC) for PYRUKYND® is $334,880.
Agios is committed to not raise the price for five years.

myAgios offers education, helps ensure access and support with compliance

Provides disease specific educational resources and product support to patient

Provides dosing & administration education to offices, including titration and tapering

For eligible uninsured or underinsured patients:

Coverage Interruption Program (Bridge)

Patient Assistance Program (PAP)

Benefit verification assistance

Prior authorization support

Appeal consultation

Education & support during interruption of coverage

All insurance-approved enrollments will be triaged to exclusive specialty pharmacy for dispense

For commercially or privately insured patients, program lowers a co-pay, coinsurance, deductible to $0

Understanding U.S. commercial opportunity: State of play today

Estimated U.S. Prevalent Pyruvate Kinase Deficiency
~3,000 (approx. midpoint)
(Range: 1,500 – 4,000)

- Estimate ~30%+ diagnosed at time of launch

Adult
~80%

Pediatric
~20%

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

% Likely Prescribed

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

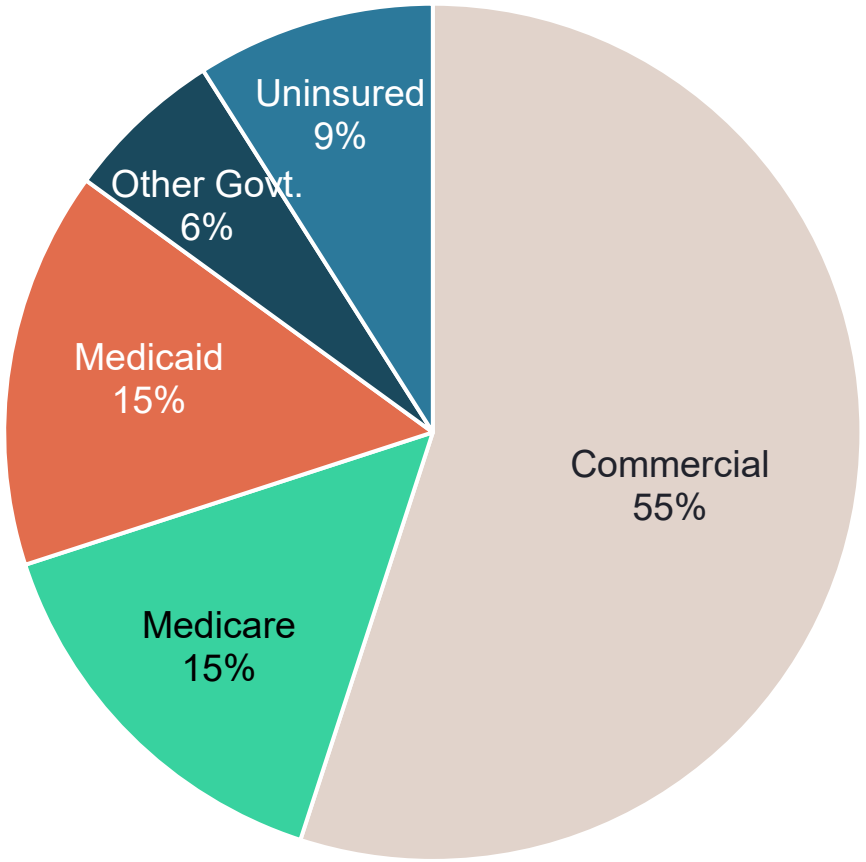
% ↑Hb ≥1.5 g/dL
~40-45%

- An additional 5% of patients will achieve improvement between 1.0 to 1.5 g/dL
- Consider likely adherence to chronic treatment

Key Details and Considerations

Ensuring effective payer engagement to ensure access for eligible patients

Anticipated Payor Mix
(% Covered Lives)

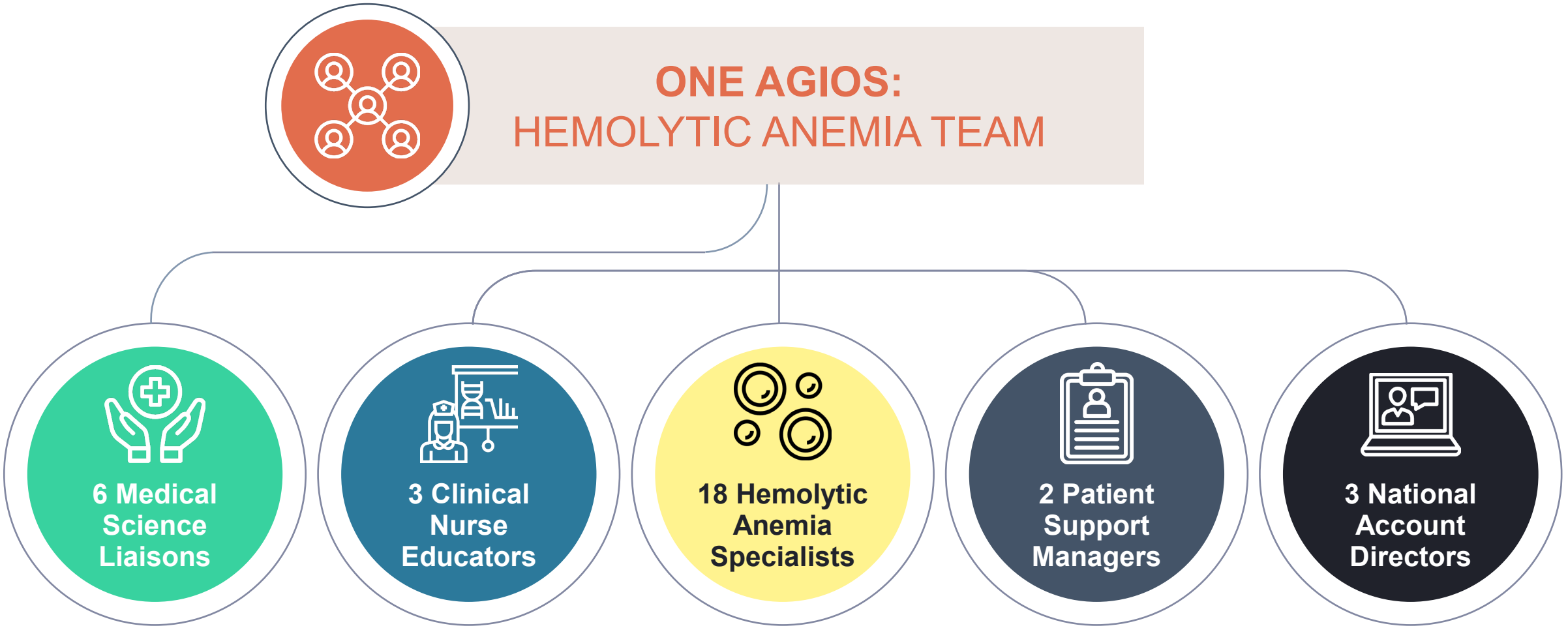


Components of Effective Payor Dialogue

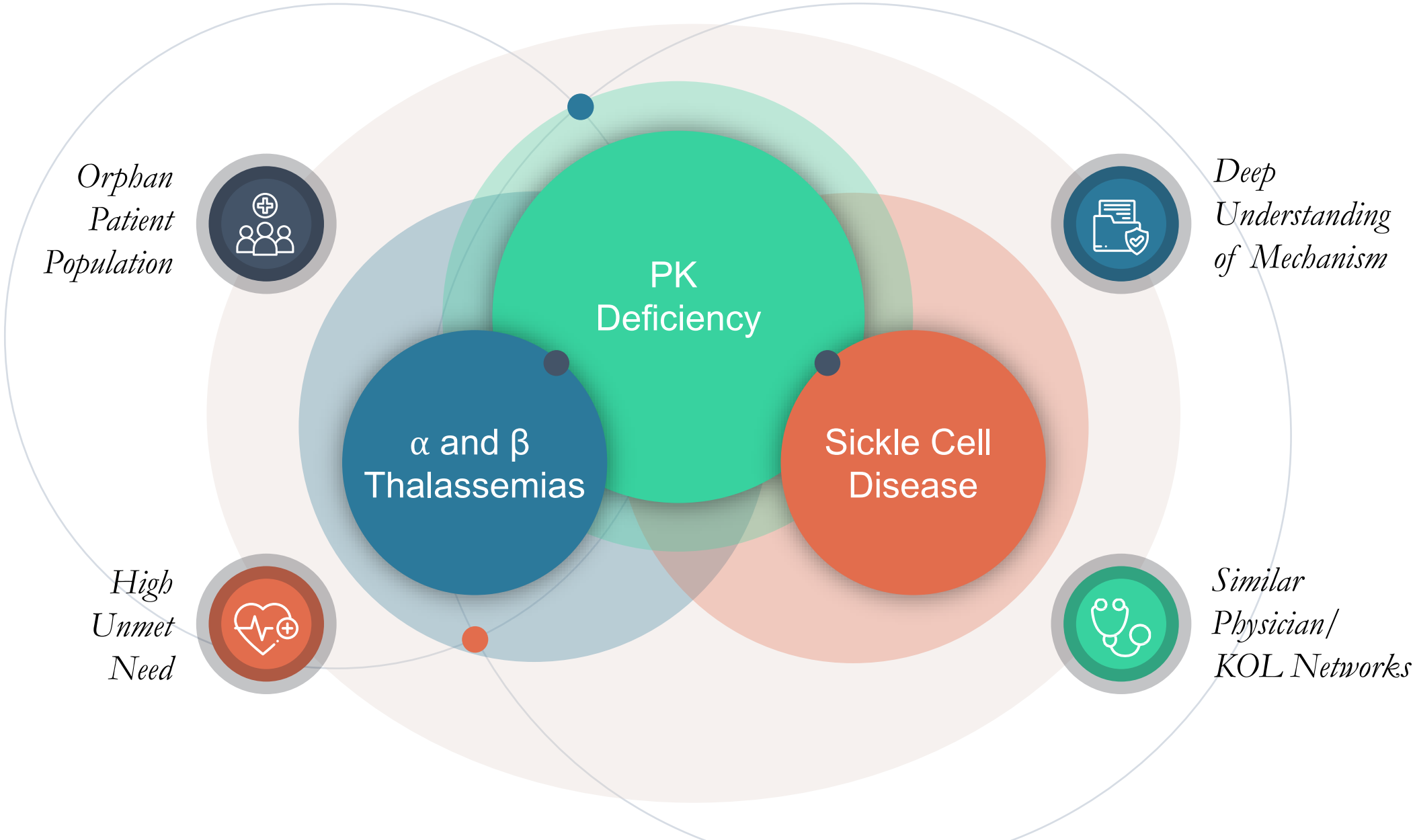
- *Unmet* Patient Need
- *Evidence of* Clinical Value
- Economic *Impact*

- Expect commercial payors to reach full formulary coverage by 1 year post-approval
  - Medical exception process in early months
- Medicare and Medicaid will lag
- Newly approved ICD-10 code will help with accelerating coverage decisions and patient profiling
- Expect routine payor requirements for initial and continued coverage

Leveraging an exceptionally talented and experienced rare disease field organization to enable launch success



Research, clinical and commercial experience with PK deficiency positions Agios well for thalassemias and sickle cell disease



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Q&A