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Fueled by Connections

40th Annual J.P. Morgan Healthcare Conference
January 12, 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 mitapivat and AG-946; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including mitapivat and AG-946; Agios' strategic vision and goals, including its 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.

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We are fueled by *connections.*

Cellular metabolism drove our start 14 years ago.

We are poised to expand our impact.

AT-A-GLANCE

FOUNDED
2008

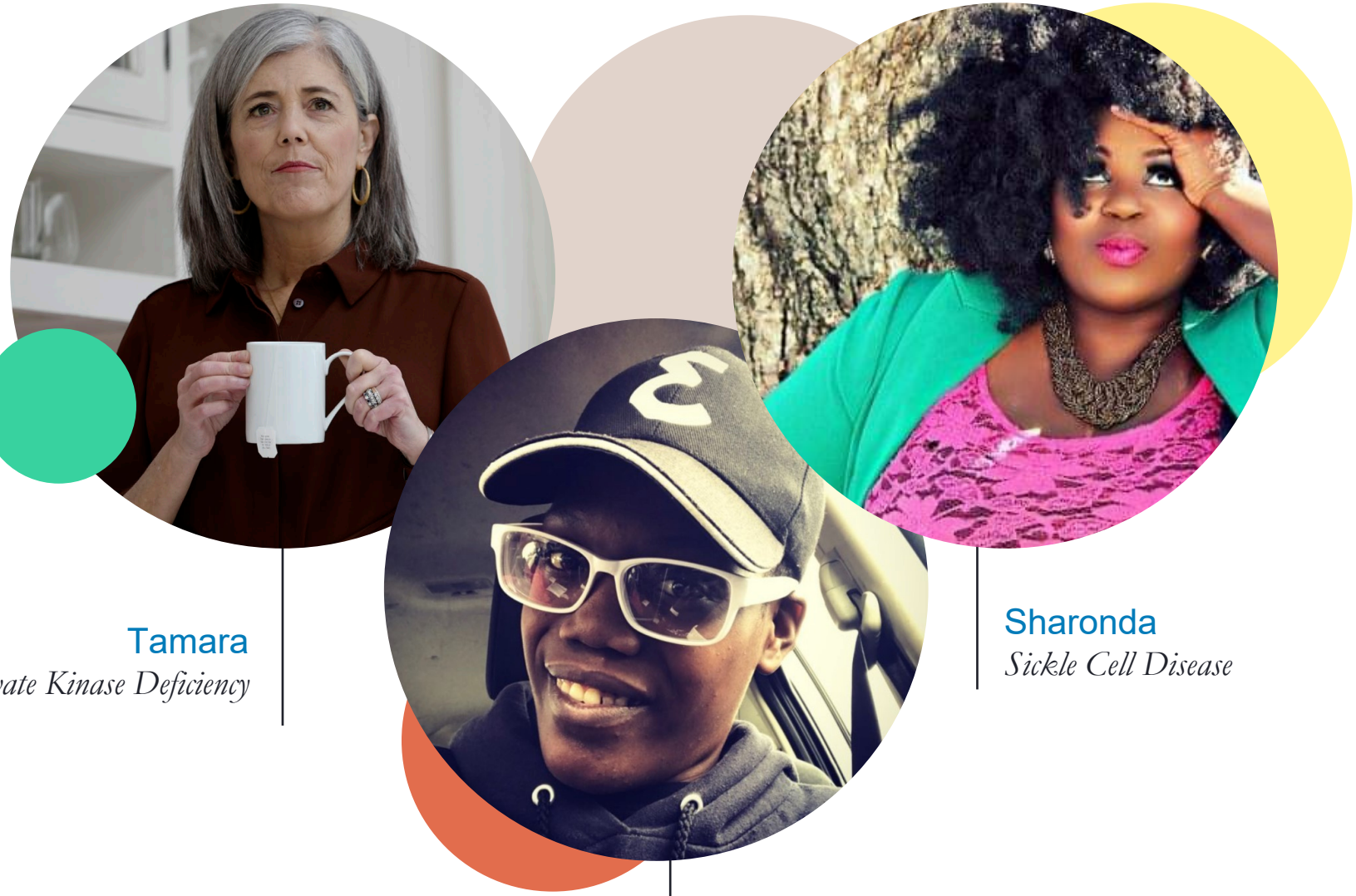
IPO
July 2013

1ST APPROVED THERAPIES
2017 & 2018

HEADQUARTERS
Cambridge, Mass.

PK ACTIVATION PROGRAMS
Pyruvate Kinase Deficiency
Thalassemia
Sickle Cell Disease

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



Tamara
Pyruvate Kinase Deficiency

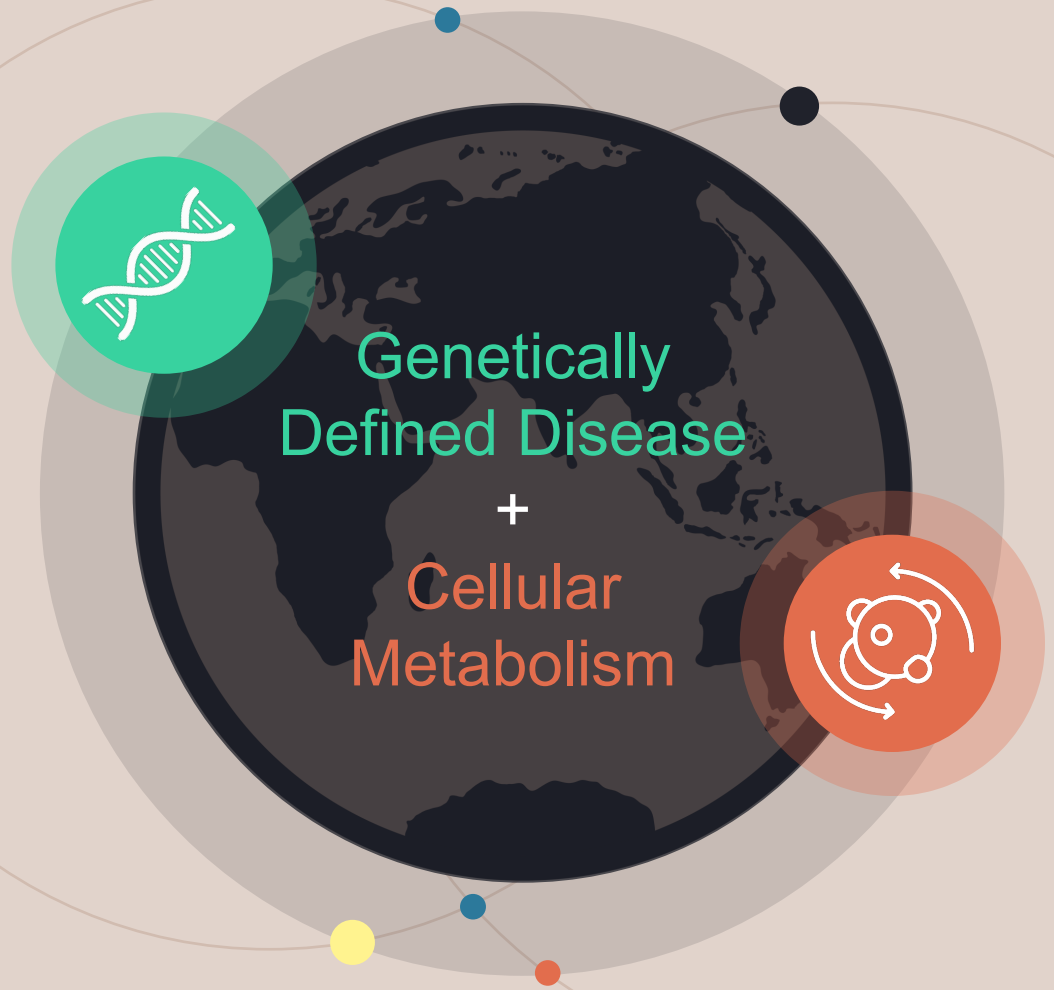
Sharonda
Sickle Cell Disease

Ryan
Thalassemia

Our strategy is anchored to our most differentiated capabilities and connectivity across research, clinical and commercial domains

Genetically Defined Disease

Genetically defined disease is a broad umbrella that encompasses both rare and more common diseases



Cellular *Metabolism*

Cellular metabolism is a central part of our heritage and scientific competency

The future of Agios is driven by *innovation* & *impact*

01 We intentionally cultivate internal and external connections

02 We have a strong balance sheet and are well capitalized to execute on our near- and long-term business strategy

03 Our unmatched expertise in cellular metabolism has yielded a pipeline with the depth, breadth and optionality to deliver sustained productivity

04 We pioneered PK activation clinical development with a differentiated approach to global development and community partnerships

05 We are ready to maximize the success of our first genetically defined disease product launch in a serious disease with no approved therapies


agios
1
Research
2
Clinical
3
Commercial

1 *Research*

2 *Clinical*

3 *Commercial*

The Agios research engine offers a unique value proposition

Deep expertise in *cellular metabolism* and genetics

- Leadership in PK activation
- Specialized lab capabilities to enable genetically defined disease studies
- A research team with significant expertise and shared desire to make a real-world impact on the lives of patients

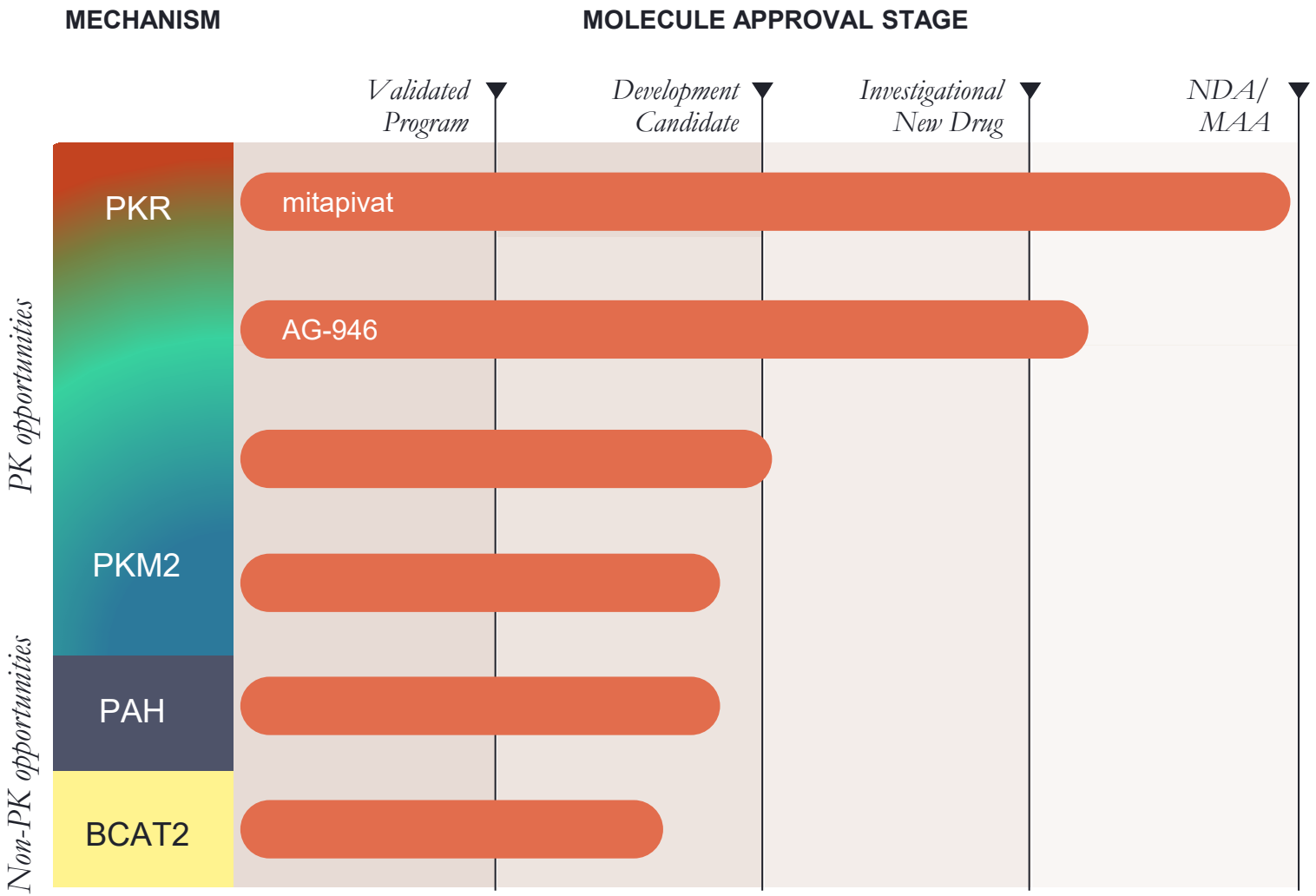
Focus on genetically defined diseases fuels *expansion of research* and biological insights

- Preclinical models that recapitulate human disease resulting in highly translatable work

Prioritize targets relevant to an *array of diseases or mutations*, creating potential for “pipelines within mechanisms”

- Preclinical exploration of both clinical-stage and novel assets in multiple indications

Our rich pipeline fuels ongoing, sustainable innovation



INDICATIONS

Pyruvate kinase activation

- Pyruvate kinase deficiency
- Sickle cell disease
- α, β−thalassemia

- Hereditary spherocytosis (~64K U.S. patients)
- Anemia of low-risk MDS (~50K U.S. patients)
- Multiple hereditary hemolytic anemias

- Renal disease
- Diabetic retinopathy and nephropathy
- Hereditary retinal indications (AMD)
- Hereditary myopathies
- Neurologic conditions

Aminoacidurias/acidemia

- Phenylketonuria (~16,500 U.S. patients)

- Methylmalonic acidemia
- Propionic acidemia

Source: Agios market research

Pipeline products are under clinical investigation, and effectiveness and safety has not been established. There is no guarantee that any pipeline product will receive health authority approval or become commercially available in any country for the use being investigated.

Our business development strategy is designed to sustain a broader portfolio and leverage Agios' core capabilities to maximize value for patients and shareholders

Ideal In-licensing Candidates

- ✓ Around IND stage
- ✓ Aligned with our therapeutic focus areas
- ✓ Ability to leverage commercial infrastructure and capabilities

Building a Portfolio of Internally and Externally Sourced Complementary Programs

Out-licensing Criteria

- ✓ Significant potential for patient impact
- ✓ Outside our core therapeutic focus areas
- ✓ Larger patient populations managed by HCP network outside current targets

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1 *Research*

2 *Clinical*

3 *Commercial*

We are the pioneering leaders in PK activation

PIVOTAL CLINICAL PROGRAMS

- ENERGIZE
- ENERGIZE-T
- ACTIVATE
- ACTIVATE-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 POSITIVE PHASE 3 READOUT IN PK DEFICIENCY
- 1st CLINICAL TRIAL EVALUATING TREATMENT IN α-THALASSEMIA

DISCOVERY	EARLY-STAGE CLINICAL DEVELOPMENT	LATE-STAGE CLINICAL DEVELOPMENT	REGULATORY SUBMISSION	APPROVAL

Pyruvate Kinase Deficiency

ACTIVATE

ACTIVATE-T

ISTs

NIH PHASE 1 SCD

a- and β-Thalassemia

PHASE 2

Healthy Volunteers / Sickle Cell Disease

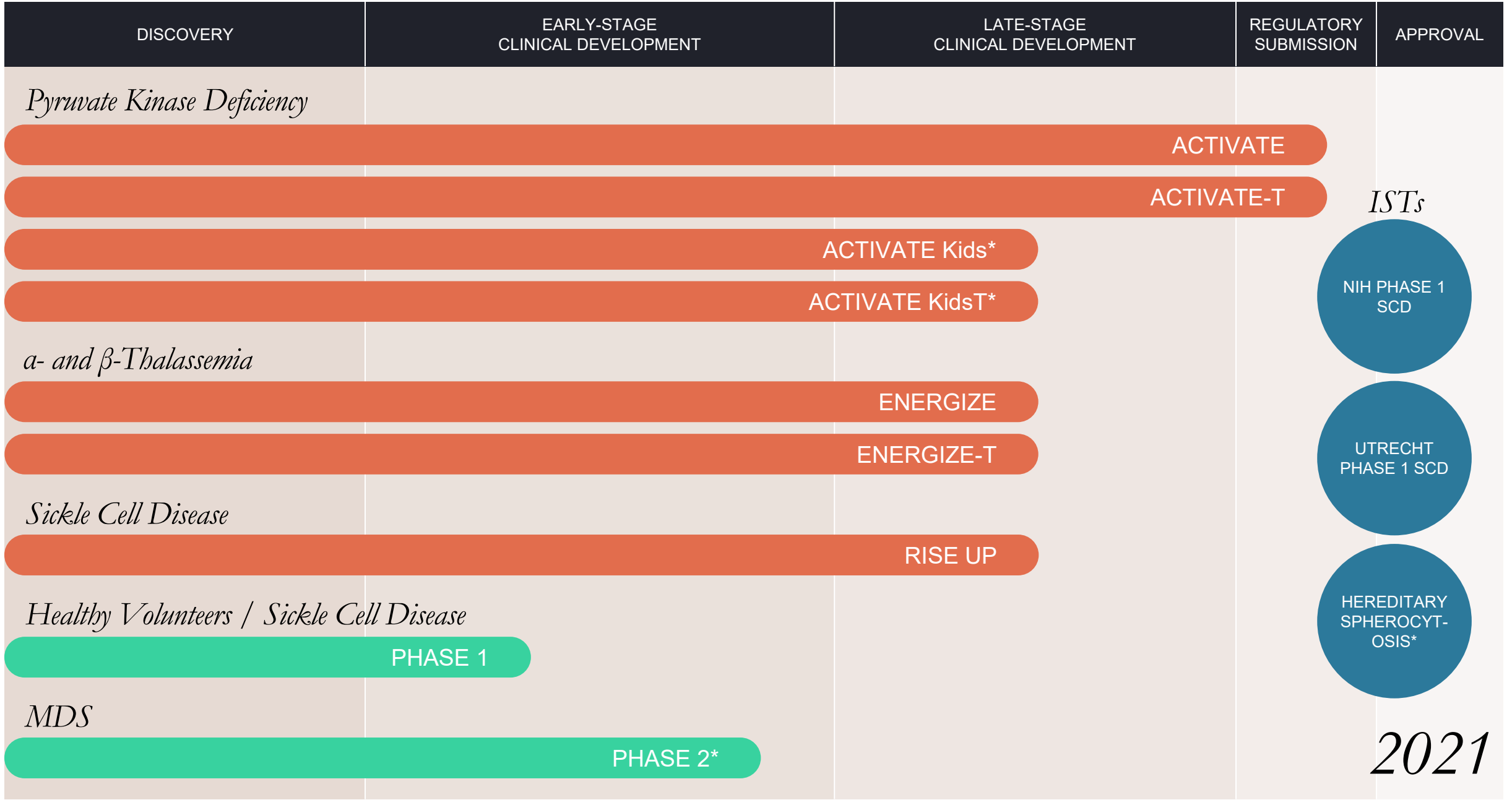
PHASE 1

2020

MITAPIVAT

AG-946

*Near-term initiation expected



MITAPIVAT AG-946 *Near-term initiation expected

Our clinical focus is to *transform the course* of hemolytic anemia by increasing red blood cell *energy, health and longevity*

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

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

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

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

Our 7+ years of clinical experience with mitapivat 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
- *Extension data* for mitapivat 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 mitapivat in adults with sickle cell disease underscore potential of mitapivat to improve clinically meaningful outcomes for patients, including anemia, hemolysis and sickling parameters
- *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

Our differentiated approach to clinical development underpinned by close, collaborative relationships

Global Reach

Solicit regulatory feedback on trial designs from the U.S. and the EU at the same time

Site selection focused on going where the patients are

Remove barriers for clinical trial participation by listening to patients all over the world

Top-notch Team

Broad industry experience throughout all levels of the clinical organization

Medical team includes academic physicians with detailed knowledge of the disease states

Where science meets heart

Extensive Network

Focus on fostering meaningful connections with the patient community

Strong ties to top KOLs across all disease states

Name recognition across industry and academia with Agios' 13+ years in hematology

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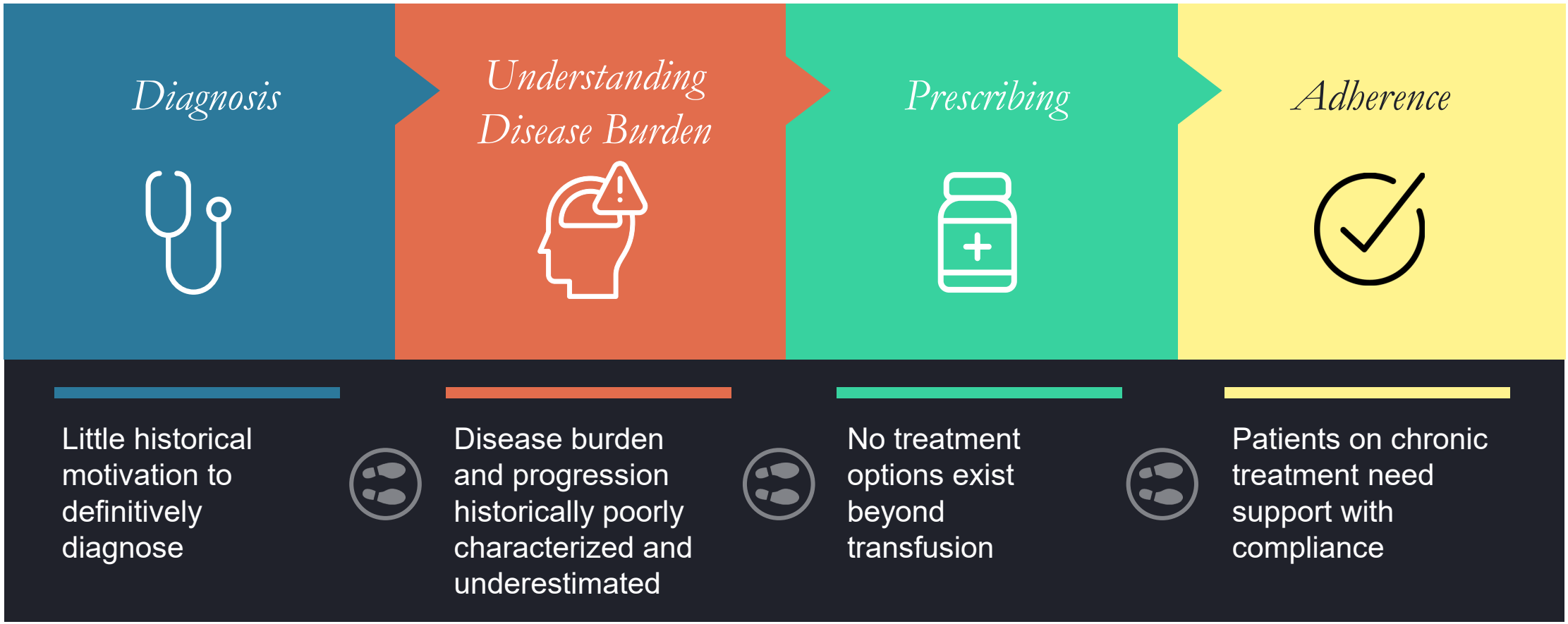
2 *Clinical*

3 *Commercial*

Commercial strategy & execution rooted in understanding the patient & provider experience in PK deficiency

Optimizing Patient & Provider Journey



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

PK Deficiency Should Be Accurately Diagnosed to Ensure Appropriate Patient Care

Identify potential patients

- 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

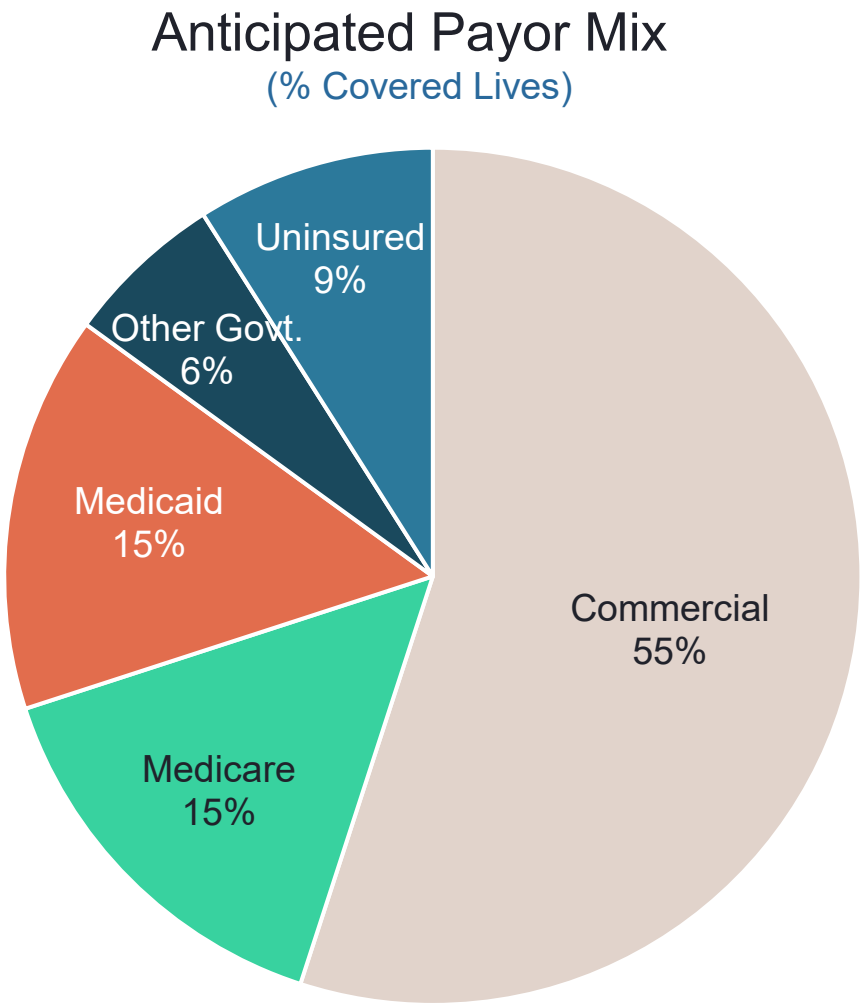
Drive awareness and urgency to manage PK deficiency

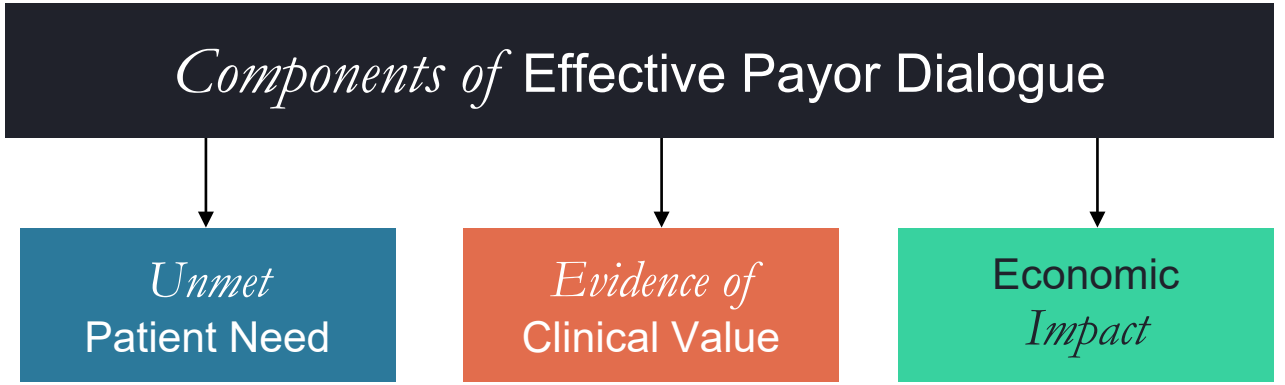
- myagios™ — Empowers patients to proactively manage their disease
- Know PK Deficiency — Disease education campaign

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

Unmet need, safety/efficacy and economic impact of greatest interest to payors; anticipate steady expansion in formulary coverage over first year post-approval





- Expect commercial payors to reach full formulary coverage by one 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

myAgios will offer streamlined, patient-oriented education and support to remove barriers to access and adherence

Challenge: Complexity, out-of-pocket costs and treatment fatigue can impact adherence

myAgios is built to make treatment start and maintenance simple for patients and providers

Provider completes enrollment form & sends to myAgios Patient Support Services

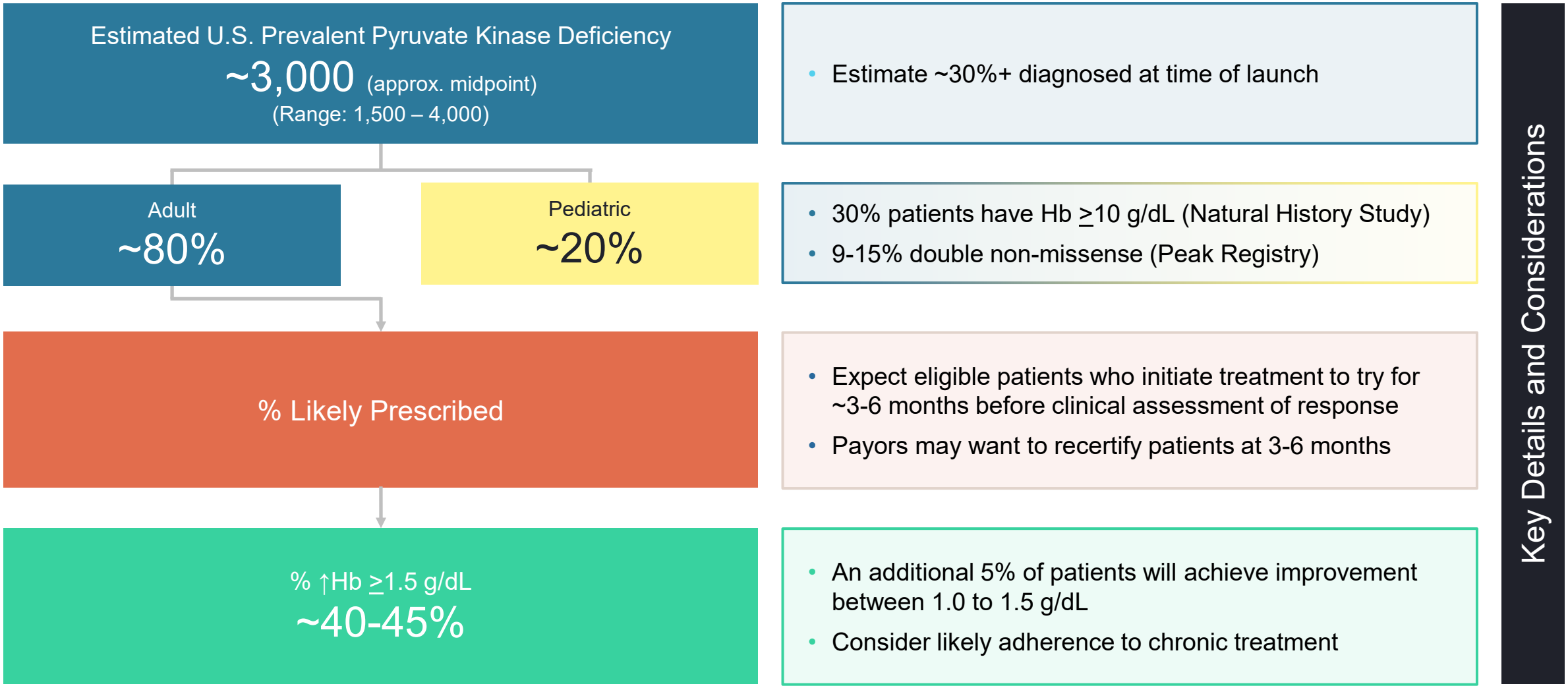
A *single* point of engagement for providers and patients

myagios™

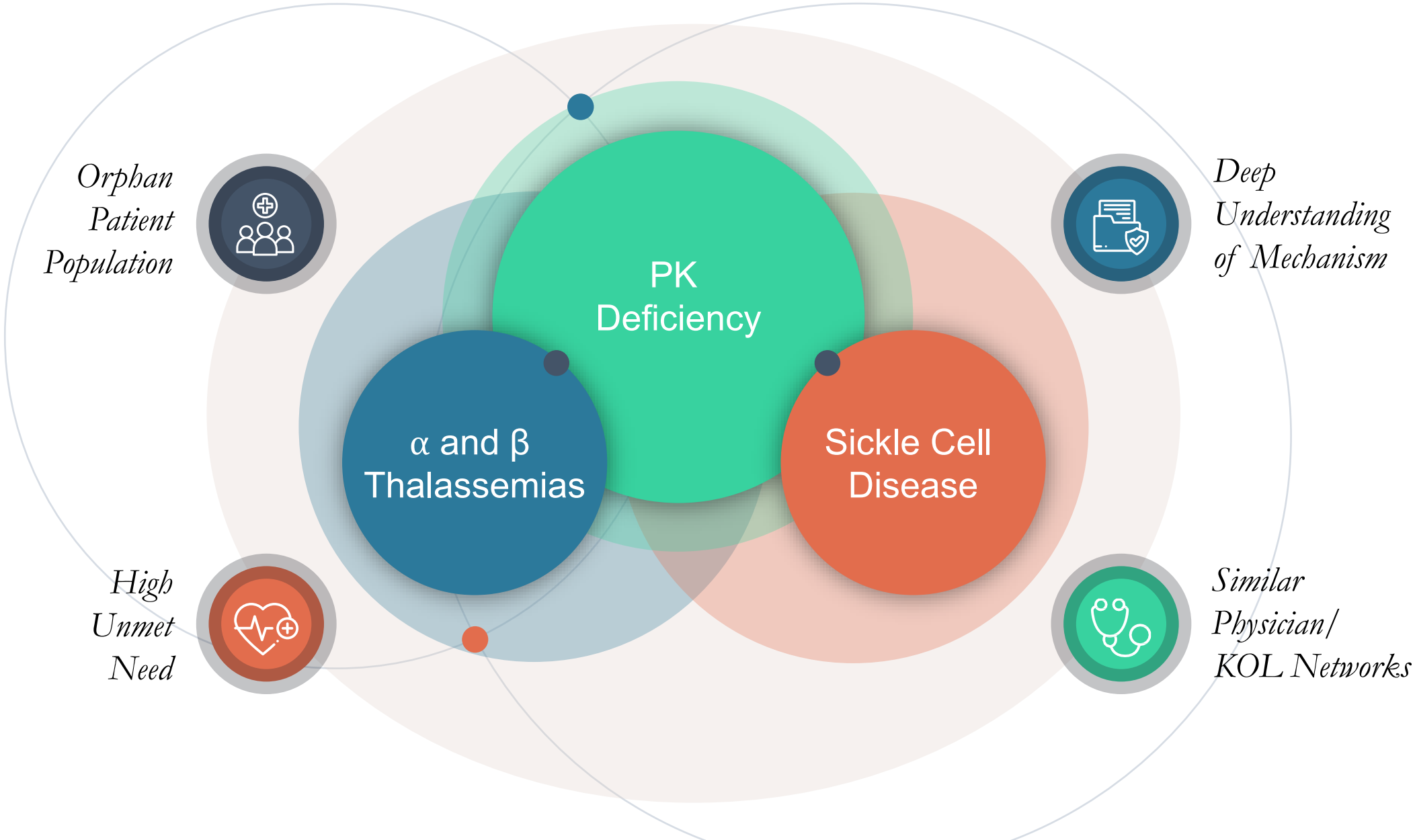
Single Specialty Pharmacy

Patient Support Manager

Understanding U.S. commercial opportunity: State of play at time of launch



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



Anticipated 2022 key milestones & priorities

Potential FDA approval and launch of mitapivat in adults with PK deficiency

PDUFA Feb. 17

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

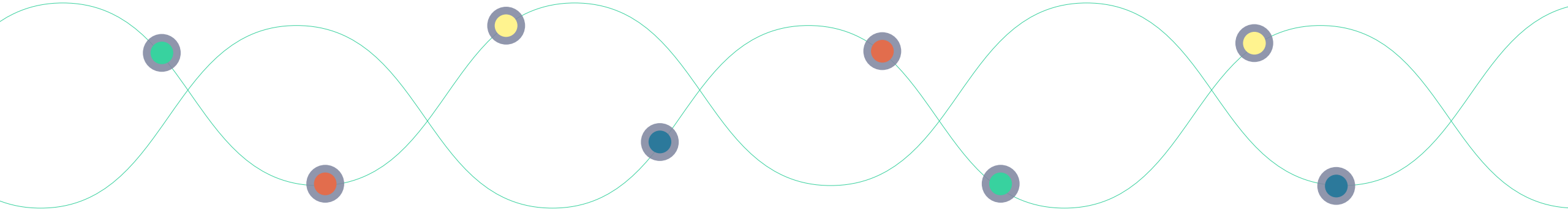
mid-2022

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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Vision 2022-2026

Building Connections. Pioneering Therapies.
Life-changing Treatments for Patients with Genetically Defined Diseases.

Mitapivat Approvals in 3 Initial Indications

5+ Molecules Exploring 10+ Indications

Pipeline Delivers a New IND Every 12-24 Months

Cash Flow Positive