THE ENERGIZE CLINICAL TRIALS

A phase 3, double-blind, randomized, placebo-controlled, multicenter study evaluating the efficacy and safety of mitapivat in subjects with non-transfusion-dependent alpha (α)- or beta (β)-thalassemia

**Primary endpoint**
Hemoglobin (Hb) response, defined as a ≥1.0 g/dL increase in average Hb concentration from Week 12 through Week 24 compared with baseline

**Key secondary endpoints**
- Change from baseline in average Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) subscale score from Week 12 through Week 24
- Change from baseline in average Hb concentration from Week 12 through Week 24

**Trial design**

<table>
<thead>
<tr>
<th>Subjects planned</th>
<th>171</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening period</td>
<td>~6 weeks</td>
</tr>
<tr>
<td>Randomization</td>
<td>2:1</td>
</tr>
<tr>
<td>Double-blind</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Open-label extension</td>
<td>Up to 5 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>100 mg of mitapivat BID</th>
<th>Placebo BID</th>
</tr>
</thead>
</table>

**Key inclusion criteria**
- ≥18 years of age at the time of providing informed consent
- Diagnosis of β-thalassemia with or without α-globin gene mutations, HbE/β-thalassemia, or α-thalassemia/HbH disease
- Hb concentration ≤10.0 g/dL
- Non-transfusion-dependent, defined as ≤5 red blood cell (RBC) units during the 24-week period before randomization, and no RBC transfusions ≤8 weeks before providing informed consent or during the screening period

**Key exclusion criteria**
- Pregnant or breastfeeding
- Documented history of homozygous or heterozygous HbS or HbC
- Certain prior or current therapies
- Significant medical condition that confers an unacceptable risk to participating in the study and/or could confound the interpretation of the study data in the opinion of the investigator

For full inclusion and exclusion criteria, as well as study locations, search ClinicalTrials.gov for NCT04770753
A phase 3, double-blind, randomized, placebo-controlled, multicenter study evaluating the efficacy and safety of mitapivat in subjects with transfusion-dependent alpha (α)– or beta (β)–thalassemia

**Primary endpoint**
Transfusion reduction response, defined as a \( \geq 50\% \) reduction in transfused RBC units with a reduction of \( \geq 2 \) units of transfused RBCs in any consecutive 12-week period through Week 48 compared with baseline

**Key secondary endpoints**
- \( \geq 33\% \) reduction in transfused RBC units from Week 13 through Week 48 compared with baseline
- \( \geq 50\% \) reduction in transfused RBC units in any consecutive 24-week period through Week 48 compared with baseline
- \( \geq 50\% \) reduction in transfused RBC units from Week 13 through Week 48 compared with baseline

**Trial design**

<table>
<thead>
<tr>
<th>Subjects planned</th>
<th>240</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening period</td>
<td>~8 weeks</td>
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<tr>
<td>Randomization</td>
<td>2:1</td>
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<tr>
<td>Double-blind</td>
<td>48 weeks</td>
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<td>Placebo BID</td>
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<tr>
<td>Open-label extension</td>
<td>Up to 5 years</td>
</tr>
</tbody>
</table>

**Key inclusion criteria**
- \( \geq 18 \) years of age at the time of providing informed consent
- Diagnosis of β-thalassemia with or without α-globin gene mutations, HbE/β-thalassemia, or α-thalassemia/HbH disease
- Transfusion-dependent, defined as 6 to 20 RBC units transfused and a \( \leq 6 \)-week transfusion-free period during the 24-week period before randomization

**Key exclusion criteria**
- Pregnant or breastfeeding
- Documented history of homozygous or heterozygous HbS or HbC
- Certain prior or current therapies
- Significant medical condition that confers an unacceptable risk to participating in the study and/or could confound the interpretation of the study data in the opinion of the investigator

For full inclusion and exclusion criteria, as well as study locations, search [ClinicalTrials.gov](https://clinicaltrials.gov) for NCT04770779