August 2017

Celgene Corporation is pleased to announce that IDHIFA is **now approved and available** for adult patients with relapsed or refractory (R/R) AML and an IDH2 mutation.

**IDHIFA EFFICACY**

IDHIFA was evaluated in an open-label, single-arm, multicenter, 2 cohort clinical trial of 199 adult patients with R/R AML and an IDH2 mutation. Patients’ IDH2 mutations were either prospectively identified by or retrospectively identified by the Abbott RealTime™ IDH2 test. IDHIFA was given orally at a starting dose of 100 mg daily until disease progression or unacceptable toxicity. Dose reductions were allowed to manage side effects. Patients had a median age of 68 years (range, 19 to 100) and received a median of 2 prior anticancer regimens (range, 1 to 6). More than half (52%) were refractory to previous therapy.

- Efficacy was established on the basis of the rate of complete response (CR)/complete response with partial hematologic recovery (CRh), the duration of CR/CRh, and the rate of conversion from transfusion dependence to transfusion independence.

**COMPLETE RESPONSE AND DURATION OF RESPONSE (N=199)**

<table>
<thead>
<tr>
<th></th>
<th>CR&lt;sup&gt;a&lt;/sup&gt;</th>
<th>CRh&lt;sup&gt;b&lt;/sup&gt;</th>
<th>CR/CRh</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td>37 (19%)</td>
<td>9 (4%)</td>
<td>46 (23%)</td>
</tr>
<tr>
<td>(95% CI, 13%-25%)</td>
<td>(95% CI, 2%-8%)</td>
<td>(95% CI, 18%-30%)</td>
<td></td>
</tr>
<tr>
<td><strong>Median DOR (months)&lt;sup&gt;c&lt;/sup&gt;</strong></td>
<td>8.2 (95% CI, 4.7-19.4)</td>
<td>9.6 (95% CI, 0.7-NA)</td>
<td>8.2 (95% CI, 4.3-19.4)</td>
</tr>
</tbody>
</table>

<sup>a</sup>CR was defined as <5% of blasts in the bone marrow, no evidence of disease, and full recovery of peripheral blood counts (platelets >100,000/μL and ANC >1,000/μL).

<sup>b</sup>CRh was defined as <5% of blasts in the bone marrow, no evidence of disease, and partial recovery of peripheral blood counts (platelets >50,000/μL and ANC >500/μL).

<sup>c</sup>DOR was defined as time since first response of CR or CRh to relapse or death, whichever is earlier.

**WARNING: DIFFERENTIATION SYNDROME**

Patients treated with IDHIFA have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, lymphadenopathy, bone pain, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

Please see additional Important Safety Information on page 5 and full Prescribing Information, including Boxed WARNING.
Of the 46 patients who achieved a best response of CR/CRh, 39 (85%) did so within 6 months of initiating IDHIFA.

**SELECTED SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS**

**Differentiation Syndrome: See Boxed WARNING.** In the clinical trial, 14% of patients treated with IDHIFA experienced differentiation syndrome. Differentiation syndrome has been observed with and without concomitant hyperleukocytosis, as early as 10 days and at up to 5 months after IDHIFA initiation. If differentiation syndrome is suspected, initiate systemic corticosteroids and hemodynamic monitoring until improvement. Taper corticosteroids only after resolution of symptoms. Differentiation syndrome symptoms may recur with premature discontinuation of corticosteroids. If severe pulmonary symptoms requiring intubation or ventilator support and/or renal dysfunction persist for more than 48 hours after initiation of corticosteroids, interrupt IDHIFA until signs and symptoms are no longer severe. Hospitalization for close observation and monitoring of patients with pulmonary and/or renal manifestation is recommended.

**Embryo-Fetal Toxicity:** Based on animal embryo-fetal toxicity studies, IDHIFA can cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with IDHIFA and for at least 1 month after the last dose. Pregnant women, patients becoming pregnant while receiving IDHIFA, or male patients with pregnant female partners should be apprised of the potential risk to the fetus.

**ADVERSE REACTIONS**

- The most common adverse reactions (≥20%) included total bilirubin increased (81%), calcium decreased (74%), nausea (50%), diarrhea (43%), potassium decreased (41%), vomiting (34%), decreased appetite (34%), and phosphorus decreased (27%)
- The most frequently reported ≥Grade 3 adverse reactions (≥5%) included total bilirubin increased (15%), potassium decreased (15%), phosphorus decreased (8%), calcium decreased (8%), diarrhea (8%), differentiation syndrome (7%), non-infectious leukocytosis (6%), tumor lysis syndrome (6%), and nausea (5%)
- Serious adverse reactions were reported in 77.1% of patients. The most frequent serious adverse reactions (≥2%) were leukocytosis (10%), diarrhea (6%), nausea (5%), vomiting (3%), decreased appetite (3%), tumor lysis syndrome (5%), and differentiation syndrome (8%). Differentiation syndrome events characterized as serious included pyrexia, renal failure acute, hypoxia, respiratory failure, and multi-organ failure.

Please see additional Important Safety Information on page 5 and full Prescribing Information, including Boxed WARNING.
**IDHIFA DOSING & ADMINISTRATION**

Starting dose:
- IDHIFA 100 mg once daily

Swallow whole with water. Do not split or crush the tablets.

Administer IDHIFA tablets orally about the same time each day.

- IDHIFA should be taken until disease progression or unacceptable toxicity
- If a dose is vomited, missed, or not taken at the usual time, administer the dose as soon as possible on the same day, and return to normal schedule the following day
- Assess blood counts and blood chemistries for leukocytosis and tumor lysis syndrome (TLS) prior to the initiation of IDHIFA and monitor at a minimum of every 2 weeks for at least the first 3 months during treatment. Manage any abnormalities promptly

**For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response**

### DOSAGE MODIFICATIONS FOR TOXICITIES

<table>
<thead>
<tr>
<th>Adverse reactions</th>
<th>Recommended action</th>
</tr>
</thead>
</table>
| **Differentiation syndrome**                                                      | - If differentiation syndrome is suspected, administer systemic corticosteroids and initiate hemodynamic monitoring  
- Interrupt IDHIFA if severe pulmonary symptoms requiring intubation or ventilator support, and/or renal dysfunction persist for more than 48 hours after initiation of corticosteroids  
- Resume IDHIFA when signs and symptoms improve to Grade 2a or lower                                                               |
| **Noninfectious leukocytosis (WBC count greater than 30 x 10^9/L)**                | - Initiate treatment with hydroxyurea, as per standard institutional practices  
- Interrupt IDHIFA if leukocytosis is not improved with hydroxyurea, and then resume IDHIFA at 100 mg daily when WBC is less than 30 x 10^9/L |
| **Elevation of bilirubin greater than 3x ULN sustained for ≥2 weeks without elevated transaminases or other hepatic disorders** | - Reduce IDHIFA dose to 50 mg daily  
- Resume IDHIFA at 100 mg daily if bilirubin elevation resolves to less than 2x ULN                                                        |
| **Other Grade 3a or higher toxicity considered related to treatment, including TLS** | - Interrupt IDHIFA until toxicity resolves to Grade 2a or lower  
- Resume IDHIFA at 50 mg daily; may increase to 100 mg daily if toxicities resolve to Grade 1a or lower  
- If Grade 3a or higher toxicity recurs, discontinue IDHIFA                                                                                  |

* Grade 1 is mild, Grade 2 is moderate, Grade 3 is serious, Grade 4 is life-threatening.  
ULN, upper limit of normal; WBC, white blood cell.

There are no contraindications to IDHIFA.

### SELECTED SAFETY INFORMATION

**LACTATION**

Many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed infants, advise women not to breastfeed during treatment with IDHIFA and for at least 1 month after the last dose.

Please see additional Important Safety Information on page 5 and full Prescribing Information, including Boxed WARNING.
Celgene Patient Support® provides:
• A single Specialist assigned to help patients in your geographic area
• Assistance with understanding patient insurance coverage for IDHIFA
• Information about financial assistance for IDHIFA

ENROLLING IN CELGENE PATIENT SUPPORT®
There are 3 simple ways to enroll in Celgene Patient Support®. Choose the option that is easiest for you.

Enroll online now. You can enroll patients in Celgene Patient Support® online. Visit www.celgenepatientsupport.com to get started

Call 1-800-931-8691. Patients can be enrolled over the phone at 1-800-931-8691, Monday–Thursday, 8 AM–7 PM ET, and Friday, 8 AM–6 PM ET (translation services available)

Email or fax the enrollment form. Download the English or Spanish enrollment form at www.celgenepatientsupport.com and return it to us by email at patientsupport@celgene.com or fax it to us at 1-800-822-2496

Learn more about IDHIFA at IDHIFAPRO.com
IDHIFA® (enasidenib) is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with an isocitrate dehydrogenase-2 (IDH2) mutation as detected by an FDA-approved test.

IMPORTANT SAFETY INFORMATION

**WARNING: DIFFERENTIATION SYNDROME**

Patients treated with IDHIFA have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, lymphadenopathy, bone pain, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

**WARNINGS AND PRECAUTIONS**

**Differentiation Syndrome: See Boxed WARNING.** In the clinical trial, 14% of patients treated with IDHIFA experienced differentiation syndrome. Differentiation syndrome has been observed with and without concomitant hyperleukocytosis, as early as 10 days and at up to 5 months after IDHIFA initiation. If differentiation syndrome is suspected, initiate systemic corticosteroids and hemodynamic monitoring until improvement. Taper corticosteroids only after resolution of symptoms. Differentiation syndrome symptoms may recur with premature discontinuation of corticosteroids. If severe pulmonary symptoms requiring intubation or ventilator support and/or renal dysfunction persist for more than 48 hours after initiation of corticosteroids, interrupt IDHIFA until signs and symptoms are no longer severe. Hospitalization for close observation and monitoring of patients with pulmonary and/or renal manifestation is recommended.

**Embryo-Fetal Toxicity:** Based on animal embryo-fetal toxicity studies, IDHIFA can cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with IDHIFA and for at least 1 month after the last dose. Pregnant women, patients becoming pregnant while receiving IDHIFA, or male patients with pregnant female partners should be apprised of the potential risk to the fetus.

**ADVERSE REACTIONS**

- The most common adverse reactions (≥20%) included total bilirubin increased (81%), calcium decreased (74%), nausea (50%), diarrhea (43%), potassium decreased (41%), vomiting (34%), decreased appetite (34%), and phosphorus decreased (27%)
- The most frequently reported ≥Grade 3 adverse reactions (≥5%) included total bilirubin increased (15%), potassium decreased (15%), phosphorus decreased (8%), calcium decreased (8%), diarrhea (8%), differentiation syndrome (7%), non-infectious leukocytosis (6%), tumor lysis syndrome (6%), and nausea (5%)
- Serious adverse reactions were reported in 77.1% of patients. The most frequent serious adverse reactions (≥2%) were leukocytosis (10%), diarrhea (6%), nausea (5%), vomiting (3%), decreased appetite (3%), tumor lysis syndrome (5%), and differentiation syndrome (8%). Differentiation syndrome events characterized as serious included pyrexia, renal failure acute, hypoxia, respiratory failure, and multi-organ failure

**LACTATION**

Many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed infants, advise women not to breastfeed during treatment with IDHIFA and for at least 1 month after the last dose.

Please see full Prescribing Information, including Boxed WARNING.