Aug. 16, 2019 – Summit, N.J. – Celgene Corporation (NASDAQ: CELG) today announced the U.S. Food and Drug Administration (FDA) has approved INREBIC® (fedratinib) for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis.1

“The approval of INREBIC is another important milestone for Celgene and underscores our commitment to people living with blood cancers,” said Jay Backstrom, M.D., M.P.H., Chief Medical Officer for Celgene. “We are excited to provide INREBIC as a new treatment option that may be used in patients with myelofibrosis, including patients previously treated with ruxolitinib.”

“Myelofibrosis can cause patients to suffer in many ways, including experiencing debilitating symptoms,” said Ruben Mesa, M.D., FACP, Director of the Mays Cancer Center, home to UT Health San Antonio MD Anderson Cancer Center. “There has not been a new treatment approved for this disease in nearly a decade. With INREBIC, physicians and patients now have another option available for myelofibrosis.”

The INREBIC development program consisted of multiple studies (including JAKARTA and JAKARTA2) in 608 patients who received more than one dose (ranging from 30 mg to 800 mg),1 of whom 459 had myelofibrosis,1 including 97 previously treated with ruxolitinib.1 The JAKARTA study evaluated the efficacy and safety of once-daily oral doses of INREBIC compared with placebo in patients with intermediate-2 or high-risk, primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis who were previously untreated with a JAK inhibitor, had enlarged spleens (a condition known as splenomegaly), and had a platelet count of ≥50 x 10^9/L (median baseline platelet count was 214 x 10^9/L; 16% <100 x 10^9/L and 84% ≥100 x 10^9/L).1,2 In the JAKARTA study, spleen volume was reduced by 35% or greater, when assessed from baseline to the end of cycle 6 (week 24), with a 4-week follow-up scan, in 37% (35 of 96) of patients treated with INREBIC 400 mg versus 1% (1 of 96) of patients who received placebo (p<0.0001).1 INREBIC also improved the Total Symptom Score as measured by the modified Myelofibrosis Symptoms Assessment Form (MFSAF) v2.0 diary (night sweats, itching, abdominal discomfort, early satiety, pain under ribs on left side, bone or muscle pain) by 50% or greater when assessed from baseline to the end of cycle 6 in 40% of (36 of 89) patients treated with 400 mg, versus 9% (7 of 81) of patients who received placebo (p<0.0001).1

INREBIC has a Boxed Warning for serious and fatal encephalopathy, including Wernicke’s. Serious encephalopathy was reported in 1.3% (8 of 608) of patients treated with INREBIC in clinical trials and 0.16% (1 of 608) of the cases were fatal. Wernicke’s encephalopathy is a neurologic emergency resulting from thiamine (Vitamin B1) deficiency. Thiamine levels should be assessed in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated.1 Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels
In the JAKARTA study, serious adverse reactions occurred in 21% of patients treated with INREBIC 400 mg once daily (n=96), with the most common (≥2%) being cardiac failure (5%) and anemia (2%). Fatal adverse reactions of cardiogenic shock occurred in 1% of patients. Permanent discontinuation due to an adverse reaction occurred in 14% of patients. The most frequent reasons for permanent discontinuation in ≥2% of patients receiving INREBIC included cardiac failure (3%), thrombocytopenia, myocardial ischemia, diarrhea, and increased blood creatinine (2% each).

Dosage interruptions due to an adverse reaction during the randomized treatment period occurred in 21% of patients who received INREBIC. Adverse reactions requiring dosage interruption in >3% of patients who received INREBIC included diarrhea and nausea. Dosage reductions due to an adverse reaction during the randomized treatment period occurred in 19% of patients who received INREBIC. Adverse reactions requiring dosage reduction in >2% of patients who received INREBIC included anemia (6%), diarrhea (3%), vomiting (3%), and thrombocytopenia (2%).

“INREBIC is a much-welcomed new treatment for the myelofibrosis community,” said Ann Brazeau, Chief Executive Officer and Founder, MPN Advocacy and Education International. “This FDA approval marks an important milestone for people living with myelofibrosis as we embark on making greater strides in the diagnosis, understanding and treatment of this disease.”

About Myelofibrosis
Myelofibrosis is a serious and rare bone marrow disorder that disrupts the body’s normal production of blood cells. Bone marrow is gradually replaced with fibrous scar tissue, which limits the ability of the bone marrow to make blood cells. The disorder can lead to anemia, weakness, fatigue and enlargement of the spleen and liver, among other symptoms. Myelofibrosis is classified as a myeloproliferative neoplasm, a group of rare blood cancers that are derived from blood-forming stem cells. In the U.S., between 16,000 and 18,500 are living with myelofibrosis, and 1.5 of every 100,000 people will be diagnosed with myelofibrosis each year. Both men and women are affected, and while the disease can affect people of all ages, the median age at diagnosis ranges from 60 to 67 years.

About JAKARTA
JAKARTA was a pivotal Phase 3, multicenter, randomized, double-blind, placebo-controlled trial evaluating the efficacy of once-daily oral doses of INREBIC compared with placebo in patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with splenomegaly and a platelet count of ≥50 x 10⁹/L (median baseline platelet count was 214 x 10⁹/L; 16% of patients had a platelet count <100 x 10⁹/L and 84% of patients had a platelet count ≥100 x 10⁹/L) who were previously untreated with a JAK inhibitor. The study included 289 patients randomized to receive either INREBIC 500 mg (n=97) or 400 mg (n=96) or placebo (n=96) across 94 sites in 24 countries.

The primary endpoint was spleen response rate, defined as the proportion of patients achieving greater than or equal to a 35% reduction from baseline in spleen volume at the end of cycle 6 as measured by magnetic resonance imaging (MRI) or computerized tomography (CT) with a follow-up scan 4 weeks later. Secondary endpoints included symptom response rate, defined as the proportion of patients with a 50% or greater reduction in Total Symptom Score when assessed from baseline to the end of cycle 6 as measured by the modified Myelofibrosis

normalize.
Symptoms Assessment Form (MFSAF) v2.0 diary\(^2\) (night sweats, itching, abdominal discomfort, early satiety, pain under ribs on left side, bone or muscle pain).\(^1\)

**About INREBIC**

INREBIC\(^\circledast\) (fedratinib) is an oral kinase inhibitor with activity against wild type and mutationally activated Janus Associated Kinase 2 (JAK2) and FMS-like tyrosine kinase 3 (FLT3). INREBIC is a JAK2-selective inhibitor with higher potency for JAK2 over family members JAK1, JAK3 and TYK2. Abnormal activation of JAK2 is associated with myeloproliferative neoplasms, including myelofibrosis and polycythemia vera. In cell models expressing mutationally active JAK2 or FLT3, INREBIC reduced phosphorylation of signal transducer and activator of transcription (STAT3/5) proteins, inhibited cell proliferation, and induced apoptotic cell death. In mouse models of JAK2\(^{V617F}\)-driven myeloproliferative disease, INREBIC blocked phosphorylation of STAT3/5, increased survival and improved disease-associated symptoms, including reduction of white blood cells, hematocrit, splenomegaly and fibrosis.\(^1\)

**INDICATION**

INREBIC\(^\circledast\) (fedratinib) is indicated for the treatment of adult patients with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF).

**IMPORTANT SAFETY INFORMATION**

**WARNING: ENCEPHALOPATHY INCLUDING WERNICKE’S**

Serious and fatal encephalopathy, including Wernicke’s, has occurred in patients treated with INREBIC. Wernicke’s encephalopathy is a neurologic emergency. Assess thiamine levels in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels normalize.

**WARNINGS AND PRECAUTIONS**

**Encephalopathy, including Wernicke’s:** Serious and fatal encephalopathy, including Wernicke’s encephalopathy, has occurred in INREBIC-treated patients. Serious cases were reported in 1.3% (8/608) of patients treated with INREBIC in clinical trials and 0.16% (1/608) of cases were fatal.

Wernicke’s encephalopathy is a neurologic emergency resulting from thiamine (Vitamin B1) deficiency. Signs and symptoms of Wernicke’s encephalopathy may include ataxia, mental status changes, and ophthalmoplegia (e.g., nystagmus, diplopia). Any change in mental status, confusion, or memory impairment should raise concern for potential encephalopathy, including Wernicke’s, and prompt a full evaluation including a neurologic examination, assessment of thiamine levels, and imaging. Assess thiamine levels in all patients prior to starting INREBIC, periodically during treatment, and as clinically indicated. Do not start INREBIC in patients with thiamine deficiency; replete thiamine prior to treatment initiation. If encephalopathy is suspected, immediately discontinue INREBIC and initiate parenteral thiamine. Monitor until symptoms resolve or improve and thiamine levels normalize.
Anemia: New or worsening Grade 3 anemia occurred in 34% of INREBIC-treated patients. The median time to onset of the first Grade 3 anemia was approximately 2 months, with 75% of cases occurring within 3 months. Mean hemoglobin levels reached nadir after 12 to 16 weeks with partial recovery and stabilization after 16 weeks. Red blood cell transfusions were received by 51% of INREBIC-treated patients and permanent discontinuation of INREBIC occurred due to anemia in 1% of patients. Consider dose reduction for patients who become red blood cell transfusion dependent.

Thrombocytopenia: New or worsening Grade ≥3 thrombocytopenia during the randomized treatment period occurred in 12% of INREBIC-treated patients. The median time to onset of the first Grade 3 thrombocytopenia was approximately 1 month; with 75% of cases occurring within 4 months. Platelet transfusions were received by 3.1% INREBIC-treated patients. Permanent discontinuation of treatment due to thrombocytopenia and bleeding that required clinical intervention both occurred in 2.1% of INREBIC-treated patients. Obtain a complete blood count (CBC) at baseline, periodically during treatment, and as clinically indicated. For Grade 3 thrombocytopenia with active bleeding or Grade 4 thrombocytopenia, interrupt INREBIC until resolved to less than or equal to Grade 2 or baseline. Restart dose at 100 mg daily below the last given dose and monitor platelets as clinically indicated.

Gastrointestinal Toxicity: Gastrointestinal toxicities are the most frequent adverse reactions in INREBIC-treated patients. During the randomized treatment period, diarrhea occurred in 66% of patients, nausea in 62% of patient and vomiting in 39% of patients. Grade 3 diarrhea 5% and vomiting 3.1% occurred. The median time to onset of any grade nausea, vomiting, and diarrhea was 1 day, with 75% of cases occurring within 2 weeks of treatment. Consider providing appropriate prophylactic anti-emetic therapy (e.g., 5-HT3 receptor antagonists) during INREBIC treatment. Treat diarrhea with anti-diarrheal medications promptly at the first onset of symptoms. Grade 3 or higher nausea, vomiting, or diarrhea not responsive to supportive measures within 48 hours, interrupt INREBIC until resolved to Grade 1 or less or baseline. Restart dose at 100 mg daily below the last given dose. Monitor thiamine levels and replete as needed.

Hepatic Toxicity: Elevations of ALT and AST (all grades) during the randomized treatment period occurred in 43% and 40%, respectively, with Grade 3 or 4 in 1% and 0%, respectively, of INREBIC-treated patients. The median time to onset of any grade transaminase elevation was approximately 1 month, with 75% of cases occurring within 3 months. Monitor hepatic function at baseline, periodically during treatment, and as clinically indicated. For Grade 3 or higher ALT and/or AST elevations (greater than 5 × ULN), interrupt INREBIC dose until resolved to Grade 1 or less or to baseline. Restart dose at 100 mg daily below the last given dose. If re-occurrence of a Grade 3 or higher elevation of ALT/AST, discontinue treatment with INREBIC.

Amylase and Lipase Elevation: Grade 3 or higher amylase 2% and/or lipase 10% elevations developed in INREBIC-treated patients. The median time to onset of any grade amylase or lipase elevation was 15 days, with 75% of cases occurring within 1 month of starting treatment. One patient developed pancreatitis in the fedratinib clinical development program (n=608) and pancreatitis resolved with treatment discontinuation. Monitor amylase and lipase at baseline, periodically during treatment, and as clinically indicated. For Grade 3 or higher amylase and/or lipase elevations, interrupt INREBIC until resolved to Grade 1 or less or to baseline. Restart dose at 100 mg daily below the last given dose.
ADVERSE REACTIONS: The most common adverse reactions for INREBIC treated vs. placebo were diarrhea (66% vs. 16%), nausea (62% vs. 15%), anemia (40% vs. 14%), and vomiting (39% vs. 5%). Dosage interruptions due to an adverse reaction during the randomized treatment period occurred in 21% of patients who received INREBIC. Adverse reactions requiring dosage interruption in >3% of patients who received INREBIC included diarrhea and nausea. Dosage reductions due to an adverse reaction during the randomized treatment period occurred in 19% of patients who received INREBIC. Adverse reactions requiring dosage reduction in >2% of patients who received INREBIC included anemia (6%), diarrhea (3%), vomiting (3%), and thrombocytopenia (2%).

DRUG INTERACTIONS: Coadministration of INREBIC with a strong CYP3A4 inhibitor increases fedratinib exposure. Increased exposure may increase the risk of adverse reactions. Consider alternative therapies that do not strongly inhibit CYP3A4 activity. Alternatively, reduce the dose of INREBIC when administering with a strong CYP3A4 inhibitor. Avoid INREBIC with strong and moderate CYP3A4 inducers. Avoid INREBIC with dual CYP3A4 and CYP2C19 inhibitor. Coadministration of INREBIC with drugs that are CYP3A4 substrates, CYP2C19 substrates, or CYP2D6 substrates increases the concentrations of these drugs, which may increase the risk of adverse reactions of these drugs. Monitor for adverse reactions and adjust the dose of drugs that are CYP3A4, CYP2C19, or CYP2D6 substrates as necessary when coadministered with INREBIC.

PREGNANCY/LACTATION: Consider the benefits and risks of INREBIC for the mother and possible risks to the fetus when prescribing INREBIC to a pregnant woman. Due to the potential for serious adverse reactions in a breastfed child, advise patients not to breastfeed during treatment with INREBIC, and for at least 1 month after the last dose.

RENAL IMPAIRMENT: Reduce INREBIC dose when administered to patients with severe renal impairment. No modification of the starting dose is recommended for patients with mild to moderate renal impairment. Due to potential increase of exposure, patients with preexisting moderate renal impairment require more intensive safety monitoring, and if necessary, dose modifications based on adverse reactions.

HEPATIC IMPAIRMENT: Avoid use of INREBIC in patients with severe hepatic impairment.

Please see full Prescribing Information, including Boxed WARNING.

About Celgene
Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through next-generation solutions in protein homeostasis, immuno-oncology, epigenetics, immunology and neuro-inflammation. For more information, please visit www.celgene.com. Follow Celgene on Social Media: @Celgene, Pinterest, LinkedIn, Facebook and YouTube.

Forward-Looking Statements
This press release contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects,"
"anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management’s current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, many of which are discussed in more detail in our Annual Report on Form 10-K and our other reports filed with the U.S. Securities and Exchange Commission, including factors related to the proposed transaction between Bristol-Myers Squibb and Celgene, such as, but not limited to, the risks that: management’s time and attention is diverted on transaction related issues; disruption from the transaction make it more difficult to maintain business, contractual and operational relationships; legal proceedings are instituted against Bristol-Myers Squibb, Celgene or the combined company that could delay or prevent the proposed transaction; and Bristol-Myers Squibb, Celgene or the combined company is unable to retain key personnel.

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