CELGENE CORPORATION ANNOUNCES POMALYST® GRANTED BREAKTHROUGH THERAPY DESIGNATION FROM FDA FOR HIV-POSITIVE AND NEGATIVE KAPOSI SARCOMA

Celgene plans to submit sNDA by end of 2019

Celgene plans additional studies with the AIDS Malignancy Consortium in U.S. and sub-Saharan Africa

SUMMIT, NJ - May. 13, 2019-- Celgene Corporation (NASDAQ: CELG) today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to POMALYST® (pomalidomide) for the treatment of patients with human immunodeficiency virus (HIV)-positive Kaposi sarcoma who have previously received systemic chemotherapy, as well as patients with HIV-negative Kaposi's sarcoma.

Kaposi sarcoma is a multicentric tumor caused by Kaposi sarcoma-associated herpesvirus, also called human herpesvirus-8. Patients suffer multiple lesions on the skin and oral mucosa, and at times other organs such as the lungs or gastrointestinal mucosa. Kaposi sarcoma most commonly arises in persons infected with HIV. There is a substantial need for new treatments because there are no approved therapies for HIV-positive patients who are refractory to or intolerant of systemic chemotherapy. Although the use of combination anti-retroviral treatments (cART or HAART) has reduced the incidence of advanced Kaposi sarcoma in the United States, there are still nearly 2000 new cases each year. The disease is more highly prevalent in areas of the world where HIV treatments are less available, such as sub-Saharan Africa, and in some countries is the most common tumor in men overall.

"The encouraging news of the FDA Breakthrough Therapy designation for POMALYST in Kaposi sarcoma reflects the urgency in accelerating the development of therapies to address diseases of this type," said Jay Backstrom, M.D., Chief Medical Officer for Celgene. "We will continue to work closely with the agency to move this program forward for patients with this rare and serious cancer."

The Breakthrough Therapy designation was granted by the FDA on the basis of the results of a clinical study performed under a Cooperative Research and Development Agreement (CRADA) by a team led by Dr. Robert Yarchoan, of the HIV and AIDS Malignancy Branch within the Center for Cancer Research of the National Cancer Institutes (NCI). The results of that study, published in the Journal of Clinical Oncology (MN Polizzotto et al, JCO, 2016, 34, 4125-31), evaluated POMALYST in patients with Kaposi sarcoma, with or without HIV infection, many of whom had received prior cytotoxic chemotherapy.

According to the FDA, Breakthrough Therapy designation is intended to expedite the development and review of medicines with early evidence of potential clinical benefit in serious diseases.

Celgene plans to submit a supplemental New Drug Application for POMALYST in this disease area by the end of 2019.

Celgene also has two additional studies planned in this disease. In partnership with the AIDS Malignancy Consortium (AMC), a U.S. multicenter study will be performed to confirm and extend the results of the

NCI study. The AMC is also sponsoring a second study in sub-Saharan Africa, where Kaposi sarcoma continues to be a serious problem. This program is a part of the Celgene Global Health effort to discover and develop new drugs for diseases that affect patients in the lower- and middle-income countries where health systems and medical resources are less advanced.

POMALYST is not approved for Kaposi sarcoma in any country.

About POMALYST

POMALYST is one of Celgene's IMiD® agents - proprietary small molecule, orally-available compounds for the treatment of some blood cancers. IMiD agents are hypothesized to have multiple mechanisms of action and have become a foundation of multiple myeloma research, with a growing number of studies exploring these compounds in different settings and diseases.

U.S. Safety Information

Indication

POMALYST® (pomalidomide) is a thalidomide analogue indicated, in combination with dexamethasone, for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy.

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY and VENOUS AND ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

- **POMALYST is contraindicated in pregnancy. POMALYST is a thalidomide analogue. Thalidomide is a known human teratogen that causes severe birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting POMALYST treatment.**
- **Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after stopping POMALYST treatment.**

POMALYST is only available through a restricted distribution program called POMALYST REMS®.

Venous and Arterial Thromboembolism

- **Deep venous thrombosis (DVT), pulmonary embolism (PE), myocardial infarction, and stroke occur in patients with multiple myeloma treated with POMALYST. Prophylactic antithrombotic measures were employed in clinical trials. Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.**

CONTRAINDICATIONS

- **Pregnancy:** POMALYST can cause fetal harm and is contraindicated in females who are pregnant. If POMALYST is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to a fetus.

WARNINGS AND PRECAUTIONS

- **Embryo-Fetal Toxicity & Females of Reproductive Potential: See Boxed WARNINGS**
  - Males: Pomalidomide is present in the semen of patients receiving the drug. Males must always use a latex or synthetic condom during any sexual contact with females of reproductive potential while taking POMALYST and for up to 4 weeks after discontinuing POMALYST, even if they have undergone a successful vasectomy. Males must not donate sperm.
  - Blood Donation: Patients must not donate blood during treatment with POMALYST and for 4 weeks following discontinuation of POMALYST therapy because the blood might be given to a pregnant female patient whose fetus must not be exposed to POMALYST.
- **POMALYST REMS® Program: See Boxed WARNINGS**
  - Prescribers and pharmacies must be certified with the **POMALYST REMS** program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive POMALYST. Patients must sign a Patient-Physician Agreement Form and comply with REMS requirements; female patients of reproductive potential who are not pregnant must comply with the pregnancy testing and contraception requirements and males must comply with contraception requirements.
  - Further information about the **POMALYST REMS** program is available at **www.CelgeneRiskManagement.com** or by telephone at 1-888-423-5436.
- **Venous and Arterial Thromboembolism: See Boxed WARNINGS.** Patients with known risk factors, including prior thrombosis, may be at greater risk, and actions should be taken to try to minimize all modifiable factors (e.g., hyperlipidemia, hypertension, smoking). Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.
- **Increased Mortality with Pembrolizumab:** In clinical trials in patients with multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.
- **Hematologic Toxicity:** Neutropenia (46%) was the most frequently reported Grade 3/4 adverse reaction in patients taking POMALYST in clinical trials, followed by anemia and thrombocytopenia. Monitor complete blood counts weekly for the first 8 weeks and monthly thereafter. Patients may require dose interruption and/or modification.
- **Hepatotoxicity:** Hepatic failure, including fatal cases, has occurred in patients treated with POMALYST. Elevated levels of alanine aminotransferase and bilirubin have also been observed in patients treated with POMALYST. Monitor liver function tests monthly. Stop POMALYST upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.

- **Severe Cutaneous Reactions Including Hypersensitivity Reactions:** Angioedema and severe cutaneous reactions including Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. DRESS may present with a cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis. Discontinue POMALYST for angioedema, skin exfoliation, bullae, or any other severe cutaneous reactions such as SJS, TEN or DRESS, and do not resume therapy.
- **Dizziness and Confusional State:** In patients taking POMALYST in clinical trials, 14% experienced dizziness (1% Grade 3 or 4) and 7% a confusional state (3% Grade 3 or 4). Instruct patients to avoid situations where dizziness or confusional state may be a problem and not to take other medications that may cause dizziness or confusional state without adequate medical advice.
- **Neuropathy:** In patients taking POMALYST in clinical trials, 18% experienced neuropathy (2% Grade 3 in one trial) and 12% peripheral neuropathy.
- **Second Primary Malignancies:** Cases of acute myelogenous leukemia have been reported in patients receiving POMALYST as an investigational therapy outside of multiple myeloma.
- **Tumor Lysis Syndrome (TLS):** TLS may occur in patients treated with POMALYST. Patients at risk are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

ADVERSE REACTIONS

The most common adverse reactions for POMALYST (≥30%) included fatigue and asthenia, neutropenia, anemia, constipation, nausea, diarrhea, dyspnea, upper-respiratory tract infections, back pain, and pyrexia.

In the phase III trial, nearly all patients treated with POMALYST + low-dose dex experienced at least one adverse reaction (99%). Adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥2% higher than control) included neutropenia (51.3%), fatigue and asthenia (46.7%), upper respiratory tract infection (31%), thrombocytopenia (29.7%), pyrexia (26.7%), dyspnea (25.3%), diarrhea (22%), constipation (21.7%), back pain (19.7%), cough (20%), pneumonia (19.3%), bone pain (18%), edema peripheral (17.3%), peripheral neuropathy (17.3%), muscle spasms (15.3%), and nausea (15%). Grade 3 or 4 adverse reactions (≥15% in the POMALYST + low-dose dex arm and ≥1% higher than control) included neutropenia (48.3%), thrombocytopenia (22%), and pneumonia (15.7%).

DRUG INTERACTIONS

Avoid concomitant use of POMALYST with strong inhibitors of CYP1A2. Consider alternative treatments. If a strong CYP1A2 inhibitor must be used, reduce POMALYST dose by 50%.

USE IN SPECIFIC POPULATIONS

- **Pregnancy: See Boxed WARNINGS.** If pregnancy does occur during treatment, immediately discontinue the drug and refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. There is a POMALYST pregnancy exposure registry that monitors pregnancy outcomes in females exposed to POMALYST during pregnancy as well as female partners of male patients who are exposed to POMALYST. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to POMALYST

to the FDA via the MedWatch program at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-423-5436.

- **Lactation:** There is no information regarding the presence of pomalidomide in human milk, the effects of POMALYST on the breastfed child, or the effects of POMALYST on milk production. Pomalidomide was excreted in the milk of lactating rats. Because many drugs are excreted in human milk and because of the potential for adverse reactions in a breastfed child from POMALYST, advise women not to breastfeed during treatment with POMALYST.
- **Pediatric Use:** Safety and effectiveness have not been established in pediatric patients.
- **Geriatric Use:** No dosage adjustment is required for POMALYST based on age. Patients >65 years of age were more likely than patients ≤65 years of age to experience pneumonia.
- **Renal Impairment:** Reduce POMALYST dose by 25% in patients with severe renal impairment requiring dialysis. Take dose of POMALYST following hemodialysis on hemodialysis days.
- **Hepatic Impairment:** Reduce POMALYST dose by 25% in patients with mild to moderate hepatic impairment and 50% in patients with severe hepatic impairment.
- **Smoking Tobacco:** Advise patients that smoking may reduce the efficacy of POMALYST. Cigarette smoking reduces the AUC of pomalidomide by 32% by CYP1A2 induction.

Please see full Prescribing Information, including Boxed WARNINGS.

About Celgene Global Health

Celgene Global Health (CGH) is a dedicated R&D unit of Celgene committed to discovering, developing and delivering novel drugs for Diseases of the Developing World (DDWs). Collaborating with non-profit and academic institutions around the globe, CGH has utilized the company's library of more than 400,000 compounds to evaluate candidates for drug development for DDWs. More than ten discovery and development programs are ongoing in several disease areas such as malaria and tuberculosis. For more information, visit https://www.celgene.com/responsibility/global-health/

About Celgene

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global pharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through gene and protein regulation. For more information, please visit the Company's website at 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. Celgene undertakes 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 other reports filed with the 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 makes it more difficult to maintain business, contractual and operational relationships; legal proceedings are instituted against Bristol-Myers Squibb, Celgene or the combined company 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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