U.S. Food and Drug Administration Approves Bristol Myers Squibb’s Pomalyset® (pomalidomide) for AIDS-Related and HIV-Negative Kaposi Sarcoma

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Pomalyset is the only oral and first new treatment option for Kaposi sarcoma in more than 20 years

Approval based on Phase 1/2 open label, single-arm clinical trial in HIV-positive and -negative adult patients with symptomatic Kaposi sarcoma

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol Myers Squibb (NYSE: BMY) today announced that Pomalyset® (pomalidomide) was approved by the U.S. Food and Drug Administration (FDA) for patients with AIDS-related Kaposi sarcoma whose disease has become resistant to highly active antiretroviral therapy (HAART), or in patients with Kaposi sarcoma who are HIV-negative. Patients with AIDS-related Kaposi sarcoma should continue HAART for their HIV as recommended by their physician. Pomalyset was granted accelerated approval, Breakthrough Therapy designation and Orphan Drug designation in these indications based on overall response rates observed in a Phase 1/2 open label, single-arm clinical trial (12-C-0047). Continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Kaposi sarcoma is a rare form of cancer that usually presents as skin lesions, but can also develop in several other areas of the body including the lungs, lymph nodes and digestive system. The disease occurs at a rate of about 6 cases per million people each year in the United States, and mostly affects people who are immunocompromised. This oral therapy is the first new treatment option available for those with Kaposi sarcoma in more than 20 years.

“Patients with Kaposi sarcoma have had few options to manage their disease for two decades,” said Diane McDowell, M.D., vice president, Hematology Global Medical Affairs, Bristol Myers Squibb. “We’re excited that the additional research into Pomalyset in this rare disease area has resulted in our ability to provide a much-needed oral treatment option for patients.”

As described in the Boxed Warnings of the prescribing information, Pomalyset can cause fetal harm and is contraindicated in females who are pregnant. Pomalyset is only available through a restricted distribution program, Pomalyset REMS®. Deep vein thrombosis, pulmonary embolism, myocardial infarction and stroke can occur in patients treated with Pomalyset and thromboprophylaxis is recommended. See additional Important Safety Information below.

“Pomalyset has shown positive results in Kaposi sarcoma patients, regardless of their HIV status,” said Robert Yarchoan, M.D., Chief of the HIV and AIDS Malignancy Branch within the Center for Cancer Research of the National Cancer Institute (NCI). “Also, it provides a therapy that is taken orally and works by a different mechanism of action than the cytotoxic chemotherapy drugs generally used to treat Kaposi sarcoma.”

About 12-C-0047

The approval of Pomalyset was based on the findings of a Phase 1/2 open-label, single-arm study conducted evaluating the safety, pharmacokinetics and efficacy of Pomalyset in patients with HIV-positive and HIV-negative symptomatic Kaposi sarcoma, the majority of whom had advanced disease. The study was 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 Institute (NCI).

A total of 28 patients (18 HIV-positive, 10 HIV-negative) received 5 mg of Pomalyset, once daily for 21 of 28-day cycles, until disease progression or unacceptable toxicity. All HIV-positive patients continued concomitant highly active antiretroviral therapy (HAART). The trial excluded patients with symptomatic pulmonary or visceral Kaposi sarcoma, history of venous or arterial thromboembolism, or procoagulant disorders. Patients received thromboprophylaxis with aspirin 81 mg once daily throughout therapy. The median time to first response was 1.8 months (0.9 to 7.6).
The primary endpoint of the study was overall response rate (ORR), which included complete response (CR), clinical complete response (cCR) and partial response (PR), as assessed by investigators according to the AIDS Clinical Trial Group (ACTG) Oncology Committee response criteria for Kaposi sarcoma. For all patients, the ORR was 71% (95% CI: 51, 87) with 14% (4/28) of patients achieving CR and 57% (16/28) of patients achieving a PR, respectively. The median duration of response for all patients was 12.1 months (95% CI: 7.6, 16.8). Additionally, half (50%) of patients who responded maintained a response at more than 12 months with Pomalyst.³

The most common adverse reactions including laboratory abnormalities (≥30%) are decreased absolute neutrophil count or white blood cells, elevated creatinine or glucose, rash, constipation, fatigue, decreased hemoglobin, platelets, phosphate, albumin, or calcium, increased ALT, nausea and diarrhea.

Adverse reactions were evaluated in 28 patients who received treatment with Pomalyst. Adverse reactions (≥20%) included maculopapular rash (71%), constipation (71%), fatigue (68%), nausea (36%), diarrhea (32%), cough (29%), dyspnea (29%), peripheral edema (29%), upper respiratory tract infection (29%), muscle spasms (25%), hypothyroidism (21%), dry skin (21%) and chills (21%). Grade 3 or 4 adverse reactions included maculopapular rash (3.6%), diarrhea (3.6%) and peripheral edema (3.6%). Grade 3 or 4 laboratory abnormalities (≥5%) worsening from baseline included decreased absolute neutrophil count (50%), decreased phosphate (25%), elevated glucose (7%) and elevated creatine kinase (7%).

Permanent discontinuation due to an adverse reaction occurred in 11% (3/28) of patients who received Pomalyst. No new safety signals were identified, and the safety of Pomalyst in Kaposi sarcoma was consistent with the known safety profile of Pomalyst in approved indications.³

About Kaposi sarcoma

Kaposi sarcoma is a rare form of cancer that usually presents as skin lesions, but can also develop in several other areas of the body including the lungs, lymph nodes and digestive system. Kaposi sarcoma is caused by Kaposi sarcoma-associated herpesvirus, also called human herpesvirus-8, and most commonly arises in persons infected with HIV who are immunocompromised. Although the use of combination anti-retroviral treatments (cART or HAART) has reduced the incidence of Kaposi sarcoma in the United States, it still occurs at a rate of approximately 6 cases per million people each year.⁵ The disease is more prevalent in areas of the world where HIV treatments are less available, and where more persons are infected with Kaposi sarcoma-associated herpesvirus, such as sub-Saharan Africa, and in some countries is the most common tumor in men overall.⁵

About Pomalyst (pomalidomide)

Indications

Pomalyst® is a thalidomide analogue indicated for the treatment of adult patients:

• in combination with dexamethasone, for patients with multiple myeloma (MM) 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.

• with AIDS-related Kaposi sarcoma (KS) after failure of highly active antiretroviral therapy (HAART) or in patients with KS who are HIV-negative. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

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 the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to a fetus.

• Hypersensitivity: Pomalyst is contraindicated in patients who have demonstrated severe hypersensitivity (e.g., angioedema, anaphylaxis) to pomalidomide or any of the excipients.

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](http://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**: In the Pomalyst multiple myeloma (MM) trials, neutropenia (46%) was the most frequently reported Grade 3 or 4 adverse reaction, 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. In the Kaposi sarcoma (KS) trial, hematologic toxicities were the most common all Grades and Grade 3 or 4 adverse reactions. Fifty percent of patients had Grade 3 or 4 neutropenia. Monitor complete blood counts every 2 weeks for the first 12 weeks and monthly thereafter. Withhold, reduce the dose or permanently discontinue Pomalyst based on the severity of the reaction.

- **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**: 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, mycarditis, and/or pericarditis. These reactions can be fatal. Consider Pomalyst interruption or discontinuation for Grade 2 or 3 skin rash. Permanently discontinue Pomalyst for Grade 4 rash, exfoliative or bullous rash, or any other severe cutaneous reactions such as SJS, TEN or DRESS.

- **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 the MM 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.

- **Hypersensitivity**: Hypersensitivity, including angioedema, anaphylaxis, and anaphylactic reactions to Pomalyst have been reported. Permanently discontinue Pomalyst for angioedema or anaphylaxis.

**ADVERSE REACTIONS**

**Multiple Myeloma:**

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%), fatigue and asthenia (47%), upper respiratory tract infection (31%), thrombocytopenia (30%), pyrexia (27%), dyspnea (25%), diarrhea (22%), constipation (22%), back pain (20%), cough (20%), pneumonia (19%), bone pain (18%), edema peripheral (17%), peripheral neuropathy (17%), muscle spasms (15%), 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%), thrombocytopenia (22%), and pneumonia (16%).

**Kaposi Sarcoma:**

The most common adverse reactions including laboratory abnormalities (≥30%) were decreased absolute neutrophil count or white blood cells, elevated creatinine or glucose, rash, constipation, fatigue, decreased hemoglobin, platelets, phosphate, albumin, or calcium, increased ALT, nausea, and diarrhea.
In the KS trial, adverse reactions were evaluated in 28 patients who received treatment with Pomalyst. Adverse reactions (N=28) ≥ 20% included maculopapular rash (71%), constipation (71%), fatigue (68%), nausea (36%), diarrhea (32%), cough (29%), dyspnea (29%), peripheral edema (29%), upper respiratory tract infection (29%), muscle spasms (25%), hypothyroidism (21%), dry skin (21%), and chills (21%). Grade 3 or 4 adverse reactions included maculopapular rash (3.6%), diarrhea (3.6%) and peripheral edema (3.6%). Grade 3 or 4 laboratory abnormalities ≥ 5% worsening from baseline included decreased absolute neutrophil (50%), elevated glucose (7%), decreased phosphate (25%) and elevated creatine kinase (7%).

**DRUG INTERACTIONS**

Avoid concomitant use of Pomalyst with strong CYP1A2 inhibitors. If concomitant use of a strong CYP1A2 inhibitor is unavoidable, reduce Pomalyst dose to 2 mg.

**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:**

  - Multiple Myeloma (MM): 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.

  - Kaposi sarcoma (KS): The clinical study did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

- **Renal Impairment:** For MM patients with severe renal impairment requiring dialysis, reduce Pomalyst dosage to 3 mg orally daily or for KS, reduce Pomalyst dosage to 4 mg orally daily. Take dose of Pomalyst following hemodialysis on hemodialysis days.

- **Hepatic Impairment:** For MM patients with mild to moderate hepatic impairment, reduce Pomalyst dosage to 3 mg orally daily and to 2 mg orally daily in patients with severe hepatic impairment. For KS in patients with mild, moderate, or severe hepatic impairment, reduce Pomalyst dosage to 3 mg orally daily.

- **Smoking Tobacco:** Advise patients that smoking may reduce the efficacy of Pomalyst. Cigarette smoking reduces pomalidomide AUC due to CYP1A2 induction.

Please see full Prescribing Information, including Boxed WARNINGS.

**Bristol Myers Squibb: Advancing Cancer Research**

At Bristol Myers Squibb, patients are at the center of everything we do. The goal of our cancer research is to increase quality, long-term survival and make cure a possibility. We harness our deep scientific experience, cutting-edge technologies and discovery platforms to discover, develop and deliver novel treatments for patients.

Building upon our transformative work and legacy in hematology and Immuno-Oncology that has changed survival expectations for many cancers, our researchers are advancing a deep and diverse pipeline across multiple modalities. In the field of immune cell therapy, this includes registrational chimeric antigen receptor (CAR) T-cell agents for numerous diseases, and a growing early-stage pipeline that expands cell and gene therapy targets, and technologies. We are developing cancer treatments directed at key biological pathways using our protein homeostasis platform, a research capability that has been the basis of our approved therapies for multiple myeloma and several promising compounds in early to mid-stage development. Our scientists are targeting different immune system pathways to address interactions between tumors, the microenvironment and the immune system to further expand upon the progress we have made and help more patients respond to treatment. Combining these approaches is key to delivering potential new options for the treatment of cancer and addressing the growing issue of resistance to immunotherapy. We source innovation internally, and in collaboration with academia, government, advocacy groups and biotechnology companies, to help make the promise of transformational medicines a reality for patients.

**About Bristol Myers Squibb**

Bristol Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube, Facebook and Instagram.

Celgene and Juno Therapeutics are wholly owned subsidiaries of Bristol-Myers Squibb Company. In certain countries outside the U.S., due to local laws, Celgene and Juno Therapeutics are referred to as Celgene, a Bristol-Myers Squibb company and Juno Therapeutics, a Bristol-Myers Squibb company.

**Bristol Myers Squibb Cautionary Statement Regarding Forward-Looking Statements**

This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 regarding, among other things, the research, development and commercialization of pharmaceutical products. All
statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on historical performance and current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect Bristol-Myers Squibb’s business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol-Myers Squibb’s Annual Report on Form 10-K for the year ended December 31, 2019, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, Bristol-Myers Squibb undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.


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$BMY announces #FDA approval of the only oral and first treatment in more than 20 years for patients with #KaposiSarcoma