May 22, 2018

Celgene to Present New and Updated Data across a Range of Blood Diseases at EHA 2018

Presentations highlight Celgene's ongoing innovative research, including the use of CAR T cell therapies to treat multiple myeloma and lymphoma, and therapies for the treatment of multiple blood disorders, including multiple myeloma, lymphoma, leukemia, myelodysplastic syndromes and beta-thalassemia

BOUDRY, Switzerland--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced that data from a broad range of early and late stage studies evaluating Celgene investigational agents and investigational uses of marketed products will be presented at the 23rd European Hematology Association (EHA) annual meeting in Stockholm, Sweden, from June 14-17, 2018.

"We are proud to be sharing new and updated data around our innovative hematological therapies at EHA 2018, which further our understanding of blood cancers and other blood-related diseases and allow us to continue to have a major impact on the lives of patients," said Nadim Ahmed, President, Hematology & Oncology Franchise. "The data presented at EHA underscore the important role of immunomodulatory drugs at various stages of multiple myeloma, as well as illustrate our ongoing work in developing innovative treatment options, such as our erythroid maturation agent and CAR T cell therapies, for patients with life threatening blood disorders and cancers."

At EHA this year, data will be presented on Revlimid in both Newly Diagnosed Multiple Myeloma and as maintenance treatment, and Pomalyst combination regimens following Revlimid use, including new data from the Phase III OPTIMISMM trial in the relapsed/refractory setting. Results from the Phase III RELEVANCE study of lenalidomide plus rituximab (R^2) versus rituximab plus chemotherapy, followed by rituximab, in previously untreated follicular lymphoma patients will be featured during the meeting's Presidential Symposium. Data will also be presented on Celgene's CAR T cell therapies, including updated findings on bb2121 in multiple myeloma and pivotal clinical data on JCAR017 in lymphoma. Additionally, 2-year safety and efficacy data on luspatercept, an investigational compound, in beta-thalassemia will be presented.

Selected abstracts include:

<u>CAR T</u>

Abstract #S138; Oral; Friday, June 15, 12.30 - 12.45, Room A8. bb2121 anti-BCMA CAR T cell therapy in patients with relapsed/refractory multiple myeloma: updated results from a multicenter Phase I study. (Raje)

Abstract #S800; Oral; Saturday, June 16, 11:45 - 12:00, Room A1. Updated safety and long term clinical outcomes in TRANSCEND NHL 001, pivotal trial of lisocabtagene maraleucel (JCAR017) in r/r aggressive NHL (Abramson)

<u>Newly-diagnosed Multiple Myeloma</u>

Abstract #PS1429; Poster Presentation; Saturday, June 16, 17:30 - 19:00. Cost comparison of treatment strategies following initiation with Rd versus VMP plus daratumumab in newly diagnosed patients ineligible for ASCT. (Jackson)

Abstract #PF570; Poster Presentation; Friday, June 15, 17:30 - 19:00. Development of a predictive model of multiple myeloma (MM) patient outcomes based on treatment (tx) sequencing using data from The Connect® MM Patient Registry. (Jagannath)

<u>Relapsed/Refractory Multiple Myeloma</u>

Abstract #S847; Oral; Saturday, June 16, 16:00 - 16:15, Room A1. OPTIMISMM: Phase III trial of pomalidomide, bortezomib, and low-dose dexamethasone vs bortezomib and low-dose dexamethasone in lenalidomide-exposed patients with relapsed or refractory multiple myeloma. (Richardson)

Abstract #PF567; Poster Presentation; Friday, June 15, 17:30 - 19:00. Safety and efficacy of pomalidomide plus low-dose dexamethasone immediately following lenalidomide-based treatment failure in patients with relapsed and/or refractory multiple myeloma. (Siegel)

Abstract #PS1292; Poster Presentation; Saturday, June 16, 17:30 - 19:00. Pomalidomide plus low-dose dexamethasone plus daratumumab in patients with relapsed and/or refractory multiple myeloma after lenalidomide-based treatment failure. (Siegel)

Abstract #PF576; Poster Presentation; Friday, June 15, 17:30 - 19:00. Safety outcomes in patients with relapsed/refractory multiple myeloma (RRMM) treated with lenalidomide for ≤ 24 months vs > 24 months in a European post-approval safety study (EU Pass). (Semenzato)

Maintenance in Multiple Myeloma

Abstract #PF562; Poster Presentation; Friday, June 15, 17:30 - 19:00. Maintenance after lenalidomide, bortezomib, and dexamethasone induction and transplant in patients with newly diagnosed multiple myeloma and high-risk cytogenetics: an enhanced medical record analysis. (Fonseca)

Acute Myeloid Leukemia

Abstract #PS980; Poster Presentation; Saturday, June 16, 17:30 - 19:00. Continuing enasidenib treatment for patients with mutant-IDH2 relapsed/refractory acute myeloid leukemia (r/r AML) with stable disease may result in improved responses and survival over time. (Stein)

Abstract #S1562; Oral; Sunday, June 17, 08:30 - 08:45, Victoria Hall. Mutant IDH (MIDH) inhibitors, ivosidenib or enasidenib, with azacitidine (AZA) in patients with acute myeloid leukemia (AML). (DiNardo)

Lymphoma

Abstract #S154; Oral; Friday, June 15, 17:00 - 17:15, Room A1. RELEVANCE: Phase III efficacy and safety study of lenalidomide plus rituximab (R^2) versus rituximab plus chemotherapy, followed by rituximab, in previously untreated follicular lymphoma. (Morschhauser)

Beta-Thalassemia

Abstract #S844; Oral; Saturday, June 16, 12:00 - 12:15, Room K2. Improvements in hemoglobin, quality of life, and six-minute-walk distance in adults with β-thalassemia treated with luspatercept: long-term Phase II study. (Piga)

The safety and efficacy of the agents and/or uses under investigation have not been established. There is no guarantee that the agents will receive health authority approval or become commercially available in any country for the uses being investigated.

A complete listing of abstracts can be found on the EHA Learning Center Web site at https://learningcenter.ehaweb.org/eha.

About Celgene's Immunomodulatory Drugs

Immunomodulatory Drugs (IMiDs®) are Celgene's proprietary small molecule, orally available compounds for the treatment of some blood cancers. IMiDs® are the foundation of multiple myeloma treatment, driven by the proven survival benefits across lines of therapy. Their mechanism of action is well defined and offers the combination of striking tumor cells, stimulating the immune system, and synergizing with other classes of treatment. With REVLIMID® (lenalidomide) and POMALYST®/IMNOVID® (pomalidomide), Celgene has a portfolio of innovative medicines that have helped transform the treatment of multiple myeloma, providing patients longer disease control at every stage of the disease from newly diagnosed to relapse refractory multiple myeloma.

About REVLIMID

REVLIMID in combination with dexamethasone (dex) is indicated for the treatment of patients with multiple myeloma (MM)

REVLIMID is indicated as maintenance therapy in patients with MM following autologous hematopoietic stem cell transplantation (auto-HSCT)

REVLIMID is indicated for the treatment of patients with transfusion-dependent anemia due to low-or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities

REVLIMID is indicated for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib

REVLIMID is not indicated and is not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY, HEMATOLOGIC TOXICITY, and VENOUS and ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

Do not use REVLIMID during pregnancy. Lenalidomide, a thalidomide analogue, caused limb abnormalities in a developmental monkey study. Thalidomide is a known human teratogen that causes severe life-threatening human birth defects. If lenalidomide is used during pregnancy, it may cause birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting REVLIMID treatment. Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after REVLIMID treatment. To avoid embryo-fetal exposure to lenalidomide, REVLIMID is only available through a restricted distribution program, the REVLIMID REMS® program.

Information about the REVLIMID REMS program is available at www.celgeneriskmanagement.com or by calling the manufacturer's toll-free number 1-888-423-5436.

Hematologic Toxicity (Neutropenia and Thrombocytopenia)

REVLIMID can cause significant neutropenia and thrombocytopenia. Eighty percent of patients with del 5q MDS had to have a dose delay/reduction during the major study. Thirty-four percent of patients had to have a second dose delay/reduction. Grade 3 or 4 hematologic toxicity was seen in 80% of patients enrolled in the study. Patients on therapy for del 5q MDS should have their complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter. Patients may require dose interruption and/or reduction. Patients may require use of blood product support and/or growth factors.

Venous and Arterial Thromboembolism

REVLIMID has demonstrated a significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), as well as risk of myocardial infarction and stroke in patients with MM who were treated with REVLIMID and dexamethasone therapy. Monitor for and advise patients about signs and symptoms of thromboembolism. Advise patients to seek immediate medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. Thromboprophylaxis is recommended and the choice of regimen should be based on an assessment of the patient's underlying risks.

CONTRAINDICATIONS

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

Severe Hypersensitivity Reactions: REVLIMID is contraindicated in patients who have demonstrated severe hypersensitivity (e.g., angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis) to lenalidomide

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity: See Boxed WARNINGS

- Females of Reproductive Potential: **See Boxed WARNINGS**
- Males: Lenalidomide 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 REVLIMID and for up to 4 weeks after discontinuing REVLIMID, even if they have undergone a successful vasectomy. Male patients taking REVLIMID must not donate sperm
- Blood Donation: Patients must not donate blood during treatment with REVLIMID and for 4 weeks following discontinuation of the drug because the blood might be given to a pregnant female patient whose fetus must not be exposed to REVLIMID

REVLIMID REMS Program: See Boxed WARNINGS: Prescribers and pharmacies must be certified with the REVLIMID REMS program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive REVLIMID. 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

Hematologic Toxicity: REVLIMID can cause significant neutropenia and thrombocytopenia. Monitor patients with neutropenia for signs of infection. Advise patients to observe for bleeding or bruising, especially with use of concomitant medications that may increase risk of bleeding. **MM:** Patients taking REVLIMID/dex or REVLIMID as maintenance therapy should have their complete blood counts (CBC) assessed every 7 days for the first 2 cycles, on days 1 and 15 of cycle 3, and every 28 days thereafter. **MDS:** Patients on therapy for del 5q MDS should have their complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter. Patients may require dose interruption and/or dose reduction. Please see the **Black Box WARNINGS** for further information. **MCL:** Patients taking REVLIMID for MCL should have their CBCs monitored weekly for the first cycle (28 days), every 2 weeks during cycles 2-4, and then monthly thereafter. Patients may require dose interruption and/or dose reduction

Venous and Arterial Thromboembolism: See Boxed WARNINGS: Venous thromboembolic events (DVT and PE) and arterial thromboses (MI and CVA) are increased in patients treated with REVLIMID. 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 regimen should be based on patient's underlying risks. ESAs and estrogens may further increase the risk of thrombosis and their use should be based on a benefit-risk decision

Increased Mortality in Patients with CLL: In a clinical trial in the first-line treatment of patients with CLL, single agent REVLIMID therapy increased the risk of death as compared to single agent chlorambucil. Serious adverse cardiovascular reactions, including atrial fibrillation, myocardial infarction, and cardiac failure, occurred more frequently in the REVLIMID arm. REVLIMID is not indicated and not recommended for use in CLL outside of controlled clinical trials

Second Primary Malignancies (SPM): In clinical trials in patients with MM receiving REVLIMID, an increase of hematologic plus solid tumor SPM, notably AML and MDS, have been observed. Monitor patients for the development of SPM. Take into account both the potential benefit of REVLIMID and risk of SPM when considering treatment

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

Hepatotoxicity: Hepatic failure, including fatal cases, has occurred in patients treated with REVLIMID/dex. Pre-existing viral liver disease, elevated baseline liver enzymes, and concomitant medications may be risk factors. Monitor liver enzymes periodically. Stop REVLIMID 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. These events can be fatal. Patients with a prior history of Grade 4 rash associated with thalidomide treatment should not receive REVLIMID. REVLIMID interruption or discontinuation should be considered for Grade 2-3 skin rash. REVLIMID must be discontinued for angioedema, Grade 4 rash, exfoliative or bullous rash, or if SJS, TEN, or DRESS is suspected and should not be resumed following discontinuation for these reactions

Tumor Lysis Syndrome (TLS): Fatal instances of TLS have been reported during treatment with lenalidomide. The patients at risk of TLS are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken

Tumor Flare Reaction (TFR): TFR has occurred during investigational use of lenalidomide for CLL and lymphoma. Monitoring and evaluation for TFR is recommended in patients with MCL. Tumor flare may mimic the progression of disease (PD). In patients with Grade 3 or 4 TFR, it is recommended to withhold treatment with REVLIMID until TFR resolves to ≤Grade 1. REVLIMID may be continued in patients with Grade 1 and 2 TFR without interruption or modification, at the physician's discretion

Impaired Stem Cell Mobilization: A decrease in the number of CD34+ cells collected after treatment (> 4 cycles) with REVLIMID has been reported. Consider early referral to transplant center to optimize timing of the stem cell collection

Thyroid Disorders: Both hypothyroidism and hyperthyroidism have been reported. Measure thyroid function before start of REVLIMID treatment and during therapy

Early Mortality in Patients with MCL: In another MCL study, there was an increase in early deaths (within 20 weeks), 12.9% in the REVLIMID arm versus 7.1% in the control arm. Risk factors for early deaths include high tumor burden, MIPI score at diagnosis, and high WBC at baseline (≥10 x 10^9/L)

ADVERSE REACTIONS

Multiple Myeloma

- **In newly diagnosed:** The most frequently reported Grade 3 or 4 reactions included neutropenia, anemia, thrombocytopenia, pneumonia, asthenia, fatigue, back pain, hypokalemia, rash, cataract, lymphopenia, dyspnea, DVT, hyperglycemia, and leukopenia. The highest frequency of infections occurred in Arm Rd Continuous (75%) compared to Arm MPT (56%). There were more Grade 3 and 4 and serious adverse reactions of infection in Arm Rd Continuous than either Arm MPT or Rd18
- The most common adverse reactions reported in ≥20% (Arm Rd Continuous): diarrhea (46%), anemia (44%), neutropenia (35%), fatigue (33%), back pain (32%), asthenia (28%), insomnia (28%), rash (26%), decreased appetite (23%), cough (23%), dyspnea (22%), pyrexia (21%), abdominal pain (21%), muscle spasms (20%), and thrombocytopenia (20%)
- **Maintenance Therapy Post Auto-HSCT:** The most frequently reported Grade 3 or 4 reactions in ≥20% (REVLIMID arm) included neutropenia, thrombocytopenia, and leukopenia. The serious adverse reactions of lung infection and neutropenia (more than 4.5%) occurred in the REVLIMID arm
- The most frequently reported adverse reactions in ≥20% (REVLIMID arm) across both maintenance studies (Study 1, Study 2) were neutropenia (79%, 61%), thrombocytopenia (72%, 24%), leukopenia (23%, 32%), anemia (21%, 9%), upper respiratory tract infection (27%, 11%), bronchitis (5%, 47%), nasopharyngitis (2%, 35%), cough (10%, 27%), gastroenteritis (0%, 23%), diarrhea (55%, 39%), rash (32%, 8%), fatigue (23%, 11%), asthenia (0%, 30%), muscle spasm (0%, 33%), and pyrexia (8%, 21%)
- **After at least one prior therapy:** The most common adverse reactions reported in ≥20% (REVLIMID/dex vs dex/placebo): fatigue (44% vs 42%), neutropenia (42% vs 6%), constipation (41% vs 21%), diarrhea (39% vs 27%), muscle cramp (33% vs 21%), anemia (31% vs 24%), pyrexia (28% vs 23%), peripheral edema (26% vs 21%), nausea (26% vs 21%), back pain (26% vs 19%), upper respiratory tract infection (25% vs 16%), dyspnea (24% vs 17%), dizziness (23% vs 17%), thrombocytopenia (22% vs 11%), rash (21% vs 9%), tremor (21% vs 7%), and weight decreased (20% vs 15%)

Myelodysplastic Syndromes

- Grade 3 and 4 adverse events reported in ≥ 5% of patients with del 5q MDS were neutropenia (53%), thrombocytopenia (50%), pneumonia (7%), rash (7%), anemia (6%), leukopenia (5%), fatigue (5%), dyspnea (5%), and back pain (5%)
- Adverse events reported in ≥15% of del 5q MDS patients (REVLIMID): thrombocytopenia (61.5%), neutropenia (58.8%), diarrhea (49%), pruritus (42%), rash (36%), fatigue (31%), constipation (24%), nausea (24%), nasopharyngitis (23%), arthralgia (22%), pyrexia (21%), back pain (21%), peripheral edema (20%), cough (20%), dizziness (20%), headache (20%), muscle cramp (18%), dyspnea (17%), pharyngitis (16%), epistaxis (15%), asthenia (15%), upper respiratory tract infection (15%)

Mantle Cell Lymphoma

- Grade 3 and 4 adverse events reported in ≥5% of patients treated with REVLIMID in the MCL trial (N=134) included neutropenia (43%), thrombocytopenia (28%), anemia (11%), pneumonia (9%), leukopenia (7%), fatigue (7%), diarrhea (6%), dyspnea (6%), and febrile neutropenia (6%)
- Adverse events reported in ≥15% of patients treated with REVLIMID in the MCL trial included neutropenia (49%), thrombocytopenia (36%), fatigue (34%), anemia (31%), diarrhea (31%), nausea (30%), cough (28%), pyrexia (23%), rash (22%), dyspnea (18%), pruritus (17%), peripheral edema (16%), constipation (16%), and leukopenia (15%)

DRUG INTERACTIONS

Periodic monitoring of digoxin plasma levels is recommended due to increased C_{max} and AUC with concomitant REVLIMID therapy. Patients taking concomitant therapies such as erythropoietin stimulating agents or estrogen containing therapies may have an increased risk of thrombosis. It is not known whether there is an interaction between dex and warfarin. Close monitoring of PT and INR is recommended in patients with MM taking concomitant warfarin

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 REVLIMID pregnancy exposure registry that monitors pregnancy outcomes in females exposed to REVLIMID during pregnancy as well as female partners of male patients who are exposed to REVLIMID. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to REVLIMID 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 lenalidomide in human milk, the effects of REVLIMID on the breastfed infant, or the effects of REVLIMID on milk production. Because many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed infants from REVLIMID, advise female patients not to breastfeed during treatment with REVLIMID
- **PEDIATRIC USE:** Safety and effectiveness have not been established in pediatric patients
- **RENAL IMPAIRMENT:** Adjust the starting dose of REVLIMID based on the creatinine clearance value and in patients on dialysis

Please see full Prescribing Information, including Boxed WARNINGS.

About IMNOVID

IMNOVID 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

- **IMNOVID is contraindicated in pregnancy. IMNOVID 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 IMNOVID treatment.**
- **Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after stopping IMNOVID treatment.**

IMNOVID 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 IMNOVID. 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:** IMNOVID can cause fetal harm and is contraindicated in females who are pregnant. If IMNOVID 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 IMNOVID and for up to 4 weeks after discontinuing IMNOVID, even if they have undergone a successful vasectomy. Males must not donate sperm.
  - Blood Donation: Patients must not donate blood during treatment with IMNOVID and for 1 month following discontinuation of IMNOVID therapy because the blood might be given to a pregnant female patient whose fetus must not be exposed to IMNOVID.
- **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 IMNOVID. 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 IMNOVID 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 IMNOVID. Elevated levels of alanine aminotransferase and bilirubin have also been observed in patients treated with IMNOVID. Monitor liver function tests monthly. Stop IMNOVID upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.
- **Hypersensitivity Reactions:** Angioedema and severe dermatologic reactions have been reported. Discontinue IMNOVID for angioedema, skin exfoliation, bullae, or any other severe dermatologic reactions, and do not resume therapy.
- **Dizziness and Confusional State:** In patients taking IMNOVID 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 IMNOVID 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 IMNOVID as an investigational therapy outside of multiple myeloma.
- **Tumor Lysis Syndrome (TLS):** TLS may occur in patients treated with IMNOVID. Patients at risk are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

ADVERSE REACTIONS

Nearly all patients treated with IMNOVID + low-dose dex experienced at least one adverse reaction (99%). The most common adverse reactions (≥15%) 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%) included neutropenia (48.3%), thrombocytopenia (22%), and pneumonia (15.7%).

DRUG INTERACTIONS

Avoid concomitant use of IMNOVID with strong inhibitors of CYP1A2. Consider alternative treatments. If a strong CYP1A2 inhibitor must be used, reduce IMNOVID 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 an IMNOVID pregnancy exposure registry that monitors pregnancy outcomes in females exposed to IMNOVID during pregnancy as well as female partners of male patients who are exposed to IMNOVID. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to IMNOVID 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 IMNOVID on the breastfed infant, or the effects of IMNOVID 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 breastfed infants from IMNOVID, advise a nursing woman to discontinue breastfeeding during treatment with IMNOVID.
- **Pediatric Use:** Safety and effectiveness have not been established in pediatric patients.
- **Geriatric Use:** No dosage adjustment is required for IMNOVID based on age. Patients > 65 years of age were more likely than patients ≤65 years of age to experience pneumonia.
- **Renal Impairment:** Reduce IMNOVID dose by 25% in patients with severe renal impairment requiring dialysis. Take dose of IMNOVID following hemodialysis on hemodialysis days.
- **Hepatic Impairment:** Reduce IMNOVID 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 IMNOVID. Cigarette smoking reduces the AUC of pomalidomide by 32% by CYP1A2 induction.

Please see full Prescribing Information**, including Boxed WARNINGS.**

About IDHIFA

IDHIFA (enasidenib) is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia with an isocitrate dehydrogenase-2 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

About Luspatercept

Luspatercept is a modified activin receptor type IIB fusion protein that acts as a ligand trap for members in the transforming growth factor-beta superfamily involved in the late stages of erythropoiesis (red blood cell production). Luspatercept regulates late-stage erythrocyte (red blood cell) precursor cell differentiation and maturation. This mechanism of action is distinct from that of erythropoietin (EPO), which stimulates the proliferation of early-stage erythrocyte precursor cells. Acceleron and Celgene are jointly developing luspatercept as part of a global collaboration. Acceleron and Celgene are enrolling Phase 3 clinical trials that are designed to evaluate the safety and efficacy of luspatercept in patients with myelodysplastic syndromes (the "MEDALIST" study) and in patients with beta-thalassemia (the "BELIEVE" study). For more information, please visit www.clinicaltrials.gov.

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.

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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 Securities and Exchange Commission.

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