Gilead Marks Fifth Approval for Trodelvy® in Metastatic Triple-Negative Breast Cancer Under Project Orbis Initiative with Health Canada Authorization

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– Antibody-Drug Conjugate Trodelvy is First Treatment to Show Survival Benefit versus Standard of Care in Metastatic Triple-Negative Breast Cancer –

– Project Orbis is a Collaborative Review Program Intended for High-Impact Oncology Products –

– Canada Joins Australia, Great Britain, Switzerland, and the United States in Approval of Trodelvy as a Second-Line Treatment Option for Adults with Metastatic TNBC –

FOSTER CITY, Calif.--(BUSINESS WIRE)--Sep. 27, 2021-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that Health Canada has approved Trodelvy® (sacituzumab govitecan-hziy) for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) who have received two or more prior therapies, at least one of them for metastatic disease. Canada joins Australia, Great Britain, Switzerland, and the United States among the countries that have approved Trodelvy for use under Project Orbis. Project Orbis is an initiative of the U.S. Food and Drug Administration (FDA) Oncology Center of Excellence (OCE) with international regulatory authorities as a global collaborative review program for high impact oncology marketing applications across participating countries.

Trodelvy is a first-in-class Trop-2 directed antibody-drug conjugate. Trop-2, a protein located on the surface of cells, is overexpressed in TNBC as well as other solid tumors. Beyond the Project Orbis regulatory approvals, the European Medicines Agency validated a Marketing Authorization Application for Trodelvy in March and regulatory review is also underway in Kazakhstan and Saudi Arabia, as well as Singapore via licensing partner, Everest Medicines.

“Because Trodelvy is the first and only targeted treatment to show benefit in overall survival in 2L metastatic TNBC versus chemotherapy, ensuring that it is accessible to eligible patients is imperative,” said Merdad Parsey, MD, PhD, Chief Medical Officer, Gilead Sciences. “We pursued innovative regulatory pathways, such as those made possible by Project Orbis, to help make Trodelvy available to patients as rapidly as possible.”

These approvals were supported by data from the Phase 3 ASCENT study, in which Trodelvy showed a statistically significant and clinically meaningful 57% reduction in the risk of disease worsening or death (progression-free survival (PFS)) and improved median PFS in patients regardless of brain metastasis to 4.8 months from 1.7 months with chemotherapy (HR: 0.43; 95% CI: 0.35-0.54; p<0.0001). Trodelvy also improved median overall survival to 11.8 months versus 6.9 months with chemotherapy (HR: 0.51; 95% CI: 0.41-0.62; p<0.0001), representing a 49% reduction in the risk of death. In the study of 2L+ TNBC patients, the most frequent Grade ≥3 treatment-related adverse events compared to single-agent chemotherapy were neutropenia (52% versus 34%), diarrhea (11% versus 1%), leukopenia (11% versus 6%) and anemia (9% versus 6%). The Trodelvy U.S. Prescribing Information has a BOXED WARNING for severe or life-threatening neutropenia and severe diarrhea; see below for Important Safety Information.

About the ASCENT Study

The ASCENT study is a global, open-label, randomized Phase 3 study that enrolled more than 500 patients across 230 study locations. The study evaluated the efficacy and safety of Trodelvy compared with a single-agent chemotherapy of the physician’s choice in patients with unresectable, locally advanced or metastatic TNBC who had received at least two prior systemic treatments. Patients were randomized to receive either Trodelvy or a chemotherapy chosen by the patients’ treating physicians. The primary endpoint was progression-free survival (PFS, as determined by blinded independent central review) in patients without brain metastases. Secondary endpoints included: PFS for full study population or intention-to-treat (ITT) population, overall survival in both the ITT population and in the subgroup without brain metastasis, independently determined objective response rate, duration of response, time to onset of response according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1), quality of life and safety. More information about ASCENT is available at http://clinicaltrials.gov/show/NCT02574455.

About Triple-Negative Breast Cancer (TNBC)

TNBC is the most aggressive type of breast cancer and accounts for approximately 15% of all breast cancers. TNBC is diagnosed more frequently in younger and premenopausal women and is more prevalent in Black and Hispanic women. TNBC cells do not have estrogen and progesterone receptors and have limited human epidermal growth factor receptor 2 (HER2). Due to the nature of TNBC, treatment options are extremely limited compared with other breast cancer types. TNBC has a higher chance of recurrence and metastases than other breast cancer types. The average time to metastatic recurrence for TNBC is approximately 2.6 years compared with 5 years for other breast cancers, and the relative five-year survival rate is much lower. Among women with metastatic TNBC, the five-year survival rate is 12%, compared with 28% for those with other types of metastatic breast cancer.

About Trodelvy

Trodelvy (sacituzumab govitecan-hziy) is a first-in-class antibody and topoisomerase inhibitor conjugate directed to the Trop-2 receptor, a protein overexpressed in multiple types of epithelial tumors, including metastatic TNBC and metastatic urothelial cancer (UC), where high expression is associated with poor survival and relapse. Beyond the approvals of Trodelvy in the United States, it is also approved for metastatic TNBC in Australia, Canada, Great Britain and Switzerland for adults with metastatic TNBC. Trodelvy is also under multiple regulatory reviews worldwide, including the EU, as well as in Singapore through our partner Everest Medicines. Trodelvy is also being developed as an investigational treatment for hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) metastatic breast cancer and metastatic non-small cell lung cancer. Additional evaluation across multiple solid tumors is also underway.

In the United States, Trodelvy is indicated for the treatment of:

- Adult patients with unresectable locally advanced or metastatic triple-negative breast cancer who have received two or more prior systemic therapies, at least one of them for metastatic disease.
- Adult patients with locally advanced or metastatic UC who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor.

U.S. Important Safety Information for Trodelvy

BOXED WARNING: NEUTROPENIA AND DIARRHEA

- **Severe or life-threatening neutropenia may occur. Withhold Trodelvy for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay.**
- **Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. Administer atropine, if not contraindicated, for early diarrhea of any severity. At the onset of late diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold Trodelvy until resolved to ≤Grade 1 and reduce subsequent doses.**

CONTRAINDICATIONS

- Severe hypersensitivity reaction to Trodelvy.

WARNINGS AND PRECAUTIONS

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur and may require dose modification. Neutropenia occurred in 61% of patients treated with Trodelvy. Grade 3-4 neutropenia occurred in 47% of patients. Febrile neutropenia occurred in 7%. Withhold Trodelvy for absolute neutrophil count below 1500/mm^3 on Day 1 of any cycle or neutrophil count below 1000/mm^3 on Day 8 of any cycle. Withhold Trodelvy for neutropenic fever.

Diarrhea: Diarrhea occurred in 65% of all patients treated with Trodelvy. Grade 3-4 diarrhea occurred in 12% of patients. One patient had intestinal perforation following diarrhea. Neutropenic colitis occurred in 0.5% of patients. Withhold Trodelvy for Grade 3-4 diarrhea and resume when resolved to ≤Grade 1. At onset, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Hypersensitivity and Infusion-Related Reactions: Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with Trodelvy. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 37% of patients. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of Trodelvy was 0.3%. The incidence of anaphylactic reactions was 0.3%. Pre-infusion medication is recommended. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Medication to treat such reactions, as well as emergency equipment, should be available for immediate use. Permanently discontinue Trodelvy for Grade 4 infusion-related reactions.

Nausea and Vomiting: Nausea occurred in 66% of all patients treated with Trodelvy and Grade 3 nausea occurred in 4% of these patients. Vomiting occurred in 39% of patients and Grade 3-4 vomiting occurred in 3% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK1 receptor antagonist as well as other drugs as indicated) for prevention of chemotherapy-induced nausea and vomiting (CINV). Withhold Trodelvy doses for Grade 3 nausea or Grade 3-4 vomiting and resume with additional supportive measures when resolved to Grade ≤1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity: Patients homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia, febrile neutropenia, and anemia and may be at increased risk for other adverse reactions with Trodelvy. The incidence of Grade 3-4 neutropenia was 67% in patients homozygous for the UGT1A1*28, 46% in patients heterozygous for the UGT1A1*28 allele and 46% in patients homozygous for the wild-type allele. The incidence of Grade 3-4 anemia was 25% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 11% in patients homozygous for the wild-type allele. Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue Trodelvy based on clinical assessment of the onset, duration and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 function.

Embryo-Fetal Toxicity: Based on its mechanism of action, Trodelvy can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. Trodelvy contains a genotoxic component, SN-38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Trodelvy and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with Trodelvy and for 3 months after the last dose.

ADVERSE REACTIONS

In the ASCENT study (IMMU-132-05), the most common adverse reactions (incidence ≥25%) were fatigue, neutropenia, diarrhea, nausea, alopecia, anemia, constipation, vomiting, abdominal pain, and decreased appetite. The most frequent serious adverse reactions (SAR) (>1%) were neutropenia (7%), diarrhea (4%), and pneumonia (3%). SAR were reported in 27% of patients, and 5% discontinued therapy due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the ASCENT study were reduced neutrophils, leukocytes, and lymphocytes.

In the TROPHY study (IMMU-132-06), the most common adverse reactions (incidence ≥25%) were diarrhea, fatigue, neutropenia, nausea, any infection, alopecia, anemia, decreased appetite, constipation, vomiting, abdominal pain, and rash. The most frequent serious adverse reactions (SAR) (≥5%) were infection (18%), neutropenia (12%, including febrile neutropenia in 10%), acute kidney injury (6%), urinary tract infection (6%), and sepsis or bacteremia (5%). SAR were reported in 44% of patients, and 10% discontinued due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the TROPHY study were reduced neutrophils, leukocytes, and lymphocytes.

DRUG INTERACTIONS

UGT1A1 Inhibitors: Concomitant administration of Trodelvy with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Avoid administering UGT1A1 inhibitors with Trodelvy.

UGT1A1 Inducers: Exposure to SN-38 may be substantially reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with Trodelvy.

Please see full Prescribing Information, including BOXED WARNING.

About Gilead Sciences

Gilead Sciences, Inc. is a biopharmaceutical company that has pursued and achieved breakthroughs in medicine for more than three decades, with the goal of creating a healthier world for all people. The company is committed to advancing innovative medicines to prevent and treat life-threatening diseases, including HIV, viral hepatitis and cancer. Gilead operates in more than 35 countries worldwide, with headquarters in Foster City, California.

Forward-Looking Statements

This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including Gilead's ability to initiate, progress or complete clinical trials within currently anticipated timelines or at all, including those involving Trodelvy; the possibility of unfavorable results from ongoing or additional trials, including those involving Trodelvy; Gilead's ability to receive regulatory approvals in a timely manner or at all, including additional regulatory approvals of Trodelvy for the treatment of metastatic TNBC, metastatic breast cancer, metastatic UC, metastatic non-small cell lung cancer and other solid tumors, and the risk that physicians may not see the benefits of prescribing Trodelvy; and any such approvals may be subject to significant limitations on use; the risk that physicians and any assumptions underlying any of the foregoing. These and other risks, uncertainties and other factors are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, as filed with the U.S. Securities and Exchange Commission. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. Investors are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties and are cautioned not to place undue reliance on these forward-looking statements. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation and disclaims any intent to update any such forward-looking statements.

*U.S. Prescribing Information for Trodelvy including **BOXED WARNING**, is available at www.gilead.com.*

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For more information about Gilead, please visit the company's website at www.gilead.com, follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

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