# The only ADC to provide significantly improved overall survival

sacituzumab govitecan-hziv 180 mg for injection

in pretreated HER2- mBC across IHC status<sup>1-3,a</sup>



based on RECIST 1.1 criteria<sup>b</sup> and OS<sup>1,2,c</sup>

ASCENT: Phase 3, randomized, active-controlled, open-label trial (N=529) that assessed PFS in brain-metastases-negative (brain-met-negative) patients by BICR based on RECIST 1.1 criteria<sup>b</sup> (see inside) and OS<sup>1,3,c</sup>

<sup>a</sup> ITT population included HER2- patients with IHC statuses of IHC 0, IHC 1+, or IHC 2+/ISH-<sup>4,5</sup> <sup>b</sup>Primary endpoint.<sup>2,3</sup> <sup>c</sup>Secondary endpoint.<sup>2,3</sup>

#### INDICATIONS

TRODELVY® (sacituzumab govitecan-hziy) is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with:

- Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.
- Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.

#### **IMPORTANT SAFETY INFORMATION**

#### **BOXED WARNING: NEUTROPENIA AND DIARRHEA**

- TRODELVY can cause severe, life-threatening, or fatal neutropenia. Withhold TRODELVY for absolute neutrophil count below 1500/mm<sup>3</sup> or neutropenic fever. Monitor blood cell counts periodically during treatment. Primary prophylaxis with G-CSF is recommended for all patients at increased risk of febrile neutropenia. Initiate antiinfective treatment in patients with febrile neutropenia without delay.
- TRODELVY can cause severe diarrhea. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of 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.

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ADC=antibody-drug conjugate; BICR=blinded independent central review; CI=confidence interval; HER2-=human epidermal growth factor receptor 2-negative; HR=hazard ratio; HR+=hormone receptor-positive; IHC=immunohistochemistry; ISH=in situ hybridization; ITT=intent-to-treat; mBC=metastatic breast cancer; mTNBC=metastatic triple-negative breast cancer; OS=overall survival; PFS=progression-free survival; RECIST=Response Evaluation Criteria in Solid Tumor; Trop-2=trophoblast cell-surface antigen-2.

## TRODELVY is the only Trop-2-directed ADC to significantly extend survival and delay disease progression in pretreated HR+/HER2-mBC<sup>1</sup>

In a prespecified descriptive analysis, **3x more** patients remained progression free at 12 months with TRODELVY versus single-agent chemotherapy<sup>2</sup>

14.4-month median OS<sup>1</sup>

Median OS was 14.4 months for

TRODELVY (95% CI: 13.0-15.7) (n=272)

versus 11.2 months with single-agent chemotherapy (95% CI: 10.1-12.7) (n=271);

HR: 0.79 (95% CI: 0.65-0.96, P=0.02)

Primary endpoint: Median PFS was 5.5 months for TRODELVY (95% CI: 4.2-7.0) (n=272) versus 4.0 months with single-agent chemotherapy (95% CI: 3.1-4.4) (n=271); HR: 0.66 (95% CI: 0.53-0.83, P=0.0003)<sup>1</sup>

12-month PFS rate was 21% with TRODELVY (95% CI: 15-28) versus 7% with single-agent chemotherapy (95% CI: 3-14).<sup>2</sup> Not powered for statistical analysis



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#### TROPiCS-02 study overview<sup>1,2,4</sup>

In the phase 3, multicenter, randomized, active-controlled, open-label trial, TRODELVY was studied versus single-agent chemotherapy. TRODELVY was studied in patients with unresectable locally advanced or metastatic HR+/HER2- breast cancer (N=543) whose disease had progressed after:

- $\geq$ 1 endocrine therapy, CDK4/6 inhibitor, and taxane in any setting (neoadjuvant, adjuvant, or metastatic)
- 2 to 4 lines of chemotherapy for metastatic disease
  - Neoadjuvant/adjuvant therapy for early-stage disease qualified as a prior line of chemotherapy if disease recurred within 12 months
- Measurable disease by RECIST 1.1

The primary endpoint was PFS by BICR based on RECIST 1.1 criteria, and select secondary endpoints included OS, QoL measures, and safety.

Patients were randomized (1:1) to receive TRODELVY 10 mg/kg as an IV infusion on Days 1 and 8 of a 21-day cycle (n=272) or physician's choice of single-agent chemotherapy (n=271), which included eribulin, vinorelbine, gemcitabine, or capecitabine. Patients were treated until disease progression or unacceptable toxicity.

#### TRODELVY offers a well-characterized safety profile in patients with pretreated HR+/HER2- mBC<sup>1</sup>

- Serious adverse reactions occurred in 28% of patients receiving TRODELVY
- Serious adverse reactions in >1% of patients receiving TRODELVY included diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%)
- TRODELVY was permanently discontinued for adverse reactions in 6% of patients. The most frequent (≥0.5%) adverse reactions leading to permanent discontinuation in patients who received TRODELVY were asthenia, general physical health deterioration, and neutropenia (each 0.7%)
- The most common (≥25%) adverse reactions, including lab abnormalities, were decreased leukocytes (88%), decreased neutrophils (83%), decreased hemoglobin (73%), decreased lymphocytes (65%), diarrhea (62%), fatigue (60%), nausea (59%), alopecia (48%), increased glucose (37%), constipation (34%), and decreased albumin (32%)
- ILD is not listed as a warning in the TRODELVY PI and there are no specific recommendations for monitoring ILD<sup>1</sup>



Scan or click for the full TROPiCS-02 study design, efficacy, and safety results

ADC=antibody-drug conjugate; BICR=blinded independent central review; CDK4/6=cyclin-dependent kinase 4/6; CI=confidence interval; HER2-=human epidermal growth factor receptor 2-negative; HR=hazard ratio; HR+=hormone receptor-positive; ILD=interstitial lung disease; IV=ntravenous; mBC=metastatic breast cancer; OS=overall survival; PFS=progression-free survival; QoL=quality of life; RECIST=Response Evaluation Criteria in Solid Tumors; Trop-2=trophoblast cell-surface antigen-2.

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TRODELVY is the only Trop-2-directed ADC to show statistically significant extended time to deterioration (TTD) of global health status/QoL compared with traditional chemotherapy<sup>6</sup>

E	EORTC QLQ-C3	0 TTD in global he Single-agent chemotherapy
TTD	Median TTD, mo (95% Cl)	Median TTD, mo (95% CI)
Global health status/QoL	4.3 (3.1-5.7) n=234	3.0 (2.2-3.9) n=207
Fatigue	2.2 (1.6-2.8) n=234	1.4 (1.1-1.9) n=205
Pain	3.8 (2.8-5.0) n=229	3.5 (2.8-5.0) n=202

- TTD of global health status/QoL, fatigue, and pain were prespecified secondary endpoints in the statistical hierarchy<sup>4,a,b</sup>
- HRQoL-evaluable patients included those in the ITT population who completed the EORTC QLQ-C30 cycle from Cycle 2, EOT visit, and at the long-term follow-up visit. Baseline mean QoL scores were comparable between both study arms<sup>4,6,7</sup>

may be confounded by events not related to disease/treatment.

<sup>a</sup> Patients who had not experienced 10-point deterioration at the time of analysis were censored on the last nonmissing assessment date. Patients without baseline or post baseline patient-reported outcome assessments were censored at the randomization date.

<sup>b</sup>TTD was defined as the time from randomization to the first date a patient achieved ≥10-point deterioration from baseline or died due to any cause, whichever occurred first.4

ADC=antibody-drug conjugate; CI=confidence interval; EORTC QLQ=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; EOT=end of treatment; HR=hazard ratio; HRQoL=health-related quality of life; ITT=intent-to-treat; OS=overall survival; QoL=quality of life; TTD=time to deterioration; Trop-2=trophoblast cell-surface antigen-2.

#### **IMPORTANT SAFETY INFORMATION (cont'd) CONTRAINDICATIONS**

Severe hypersensitivity reaction to TRODELVY.

#### WARNINGS AND PRECAUTIONS

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur as early as the first cycle of treatment and may require dose modification. Neutropenia occurred in 64% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6%. Neutropenic colitis occurred in 1.4%. Primary prophylaxis with G-CSF is recommended starting in the first cycle of treatment in all patients at increased risk of febrile neutropenia, including older patients, patients with previous neutropenia, poor performance status, organ dysfunction, or multiple comorbidities. Monitor absolute neutrophil count (ANC) during treatment. Withhold TRODELVY for absolute ANC below 1500/mm<sup>3</sup> on Day 1 of any cycle or below 1000/mm<sup>3</sup> on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Treat neutropenia with G-CSF and administer prophylaxis in subsequent cycles as clinically indicated or indicated in Table 2 of USPI.

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at baseline and at least 1 post baseline visit, with HRQoL assessed at baseline, Day 1 of each treatment

#### Limitation: EORTC QLQ-C30 is not all-inclusive and does not include adequate assessment of additional expected treatment-related symptoms or overall side effect bother from the patient perspective. The results should be interpreted with caution due to the open-label design of the study and because TTD

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# TRODELVY is the only ADC with statistically significant OS compared to single-agent chemotherapy in pretreated 2L+ mTNBC—with mOS ~2x longer<sup>1</sup>



Primary endpoint: In the primary analysis (brain-met-negative) population, TRODELVY demonstrated statistically significant median PFS results versus single-agent chemotherapy<sup>3</sup>:

 Median PFS was 5.6 months with TRODELVY (95% Cl: 4.3-6.3) (n=235) versus 1.7 months with single-agent chemotherapy (95% CI: 1.5-2.6) (n=233); HR: 0.41 (95% CI: 0.32-0.52, P<0.001)

~1 YEAR median overall survival (OS)<sup>1</sup> Median OS in the full population<sup>1</sup> ~2x LONGER TRODELVY Single-agent chemotherapy 0 1 2 3 4 5 6 7 8 9 10 11 12 MONTHS 11.8 months with TRODELVY (95% CI: 10.5-13.8) (n=267) versus 6.9 months with single-agent chemotherapy (95% CI: 5.9-7.6) (n=262); HR: 0.51 (95% CI: 0.41-0.62, P<0.0001)<sup>1</sup>

In the brain-met-negative population, TRODELVY demonstrated statistically significant improvement in median OS versus single-agent chemotherapy<sup>3</sup>:

 Median OS was 12.1 months with TRODELVY (95% CI: 10.7-14.0) (n=235) versus 6.7 months with single-agent chemotherapy (95% CI: 5.8-7.7) (n=233); HR: 0.48 (95% CI: 0.38-0.59, P<0.001)

2L=second line; ADC=antibody-drug conjugate; brain-met-negative=brain-metastases-negative; CI=confidence interval; HR=hazard ratio; mOS= median overall survival; mTNBC=metastatic triple-negative breast cancer; OS=overall survival; PFS=progression-free survival.

#### **IMPORTANT SAFETY INFORMATION (cont'd)**

#### WARNINGS AND PRECAUTIONS (cont'd)

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Diarrhea: Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 11% of patients. One patient had intestinal perforation following diarrhea. Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all 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: TRODELVY can cause serious hypersensitivity reactions including life-threatening anaphylactic reactions. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 35% of patients. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.2%. The incidence of anaphylactic reactions was 0.2%. Pre-infusion medication is recommended. Have medications and emergency equipment to treat such reactions available for immediate use. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

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# ASCENT: A landmark phase 3 trial assessing survival in more than 500 patients with pretreated mTNBC<sup>1,3</sup>



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ASCENT study overview<sup>1,3</sup>

In the phase 3, randomized, active-controlled, open-label trial, TRODELVY was evaluated versus single-agent chemotherapy.

TRODELVY was studied in patients with unresectable locally advanced or mTNBC who had relapsed after at least 2 prior chemotherapies, at least 1 of them for metastatic disease.

The primary endpoint was PFS in brain-metastases-negative (brain-met-negative) patients by BICR based on RECIST 1.1 criteria (primary endpoint), and select secondary endpoints included PFS for the full population (all patients with and without brain metastases) and OS.

Patients were randomized (1:1) to receive TRODELVY 10 mg/kg as an IV infusion on Days 1 and 8 of a 21-day cycle (n=267) or physician's choice of single-agent chemotherapy (n=262). Patients were treated until disease progression or unacceptable toxicity.

In the TRODELVY group, 13% of patients received only 1 prior line of systemic therapy in the metastatic setting, and efficacy results were consistent with those who received at least 2 prior lines in the metastatic setting. In the full population, 88% of patients were brain-met negative (n=468; 235 in the TRODELVY arm and 233 in the single-agent chemotherapy arm).

#### A well-characterized safety profile in pretreated 2L+ mTNBC<sup>1</sup>

- Serious adverse reactions occurred in 27% of patients receiving TRODELVY
- diarrhea (4%), and pneumonia (3%)
- were pneumonia (1%) and fatigue (1%)
- decreased potassium (33%), increased albumin (32%), abdominal pain (30%), decreased appetite (28%), increase aspartate aminotransferase (27%), increased alanine aminotransferase (26%), increased alkaline phosphatase (26%), and decreased phosphate (26%)
- ILD is not listed as a warning in the TRODELVY PI and there are no specific recommendations for monitoring ILD<sup>1</sup>

BICR=blinded independent central review; IV=intravenous; mTNBC=metastatic triple-negative breast cancer; 0S=overall survival; PFS=progression-free survival; RECIST=Response Evaluation Criteria in Solid Tumors.

### IMPORTANT SAFETY INFORMATION (cont'd)

#### WARNINGS AND PRECAUTIONS (cont'd)

Nausea and Vomiting: TRODELVY is emetogenic and can cause severe nausea and vomiting. Nausea occurred in 64% of all patients treated with TRODELVY and Grade 3-4 nausea occurred in 3% of these patients. Vomiting occurred in 35% of patients and Grade 3-4 vomiting occurred in 2% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK, 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  $\leq$ 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.

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sacituzumab govitecan-hziy

180 mg for injection

Serious adverse reactions in >1% of patients receiving TRODELVY included neutropenia (7%),

• TRODELVY was permanently discontinued for adverse reactions in 5% of patients. Adverse reactions leading to permanent discontinuation in  $\geq$ 1% of patients who received TRODELVY

 The most common (≥25%) adverse reactions, including lab abnormalities, were decreased hemoglobin (94%), decreased lymphocyte count (88%), decreased leukocyte count (86%), decreased neutrophil count (78%), fatigue (65%), diarrhea (59%), nausea (57%), increased glucose (49%), alopecia (47%), constipation (37%), decreased calcium (36%), vomiting (33%), decreased magnesium (33%),



Scan or click for the full ASCENT study design, efficacy, and safety results

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#### IMPORTANT SAFETY INFORMATION (cont'd)

#### WARNINGS AND PRECAUTIONS (cont'd)

**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 58% in patients homozygous for the UGT1A1\*28, 49% in patients heterozygous for the UGT1A1\*28 allele, and 43% in patients homozygous for the wild-type allele. The incidence of Grade 3-4 anemia was 21% in patients homozygous for the UGT1A1\*28 allele, 10% in patients heterozygous for the UGT1A1\*28 allele, and 9% 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 pooled safety population, the most common (≥25%) adverse reactions including laboratory abnormalities were decreased leukocyte count (84%), decreased neutrophil count (75%), decreased hemoglobin (69%), diarrhea (64%), nausea (64%), decreased lymphocyte count (63%), fatigue (51%), alopecia (45%), constipation (37%), increased glucose (37%), decreased albumin (35%), vomiting (35%), decreased appetite (30%), decreased creatinine clearance (28%), increased alkaline phosphatase (28%), decreased magnesium (27%), decreased potassium (26%), and decreased sodium (26%).

In the ASCENT study (locally advanced or metastatic triple-negative breast cancer), the most common adverse reactions (incidence  $\geq$ 25%) were fatigue, diarrhea, nausea, alopecia, 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  $\geq$ 25%) in the ASCENT study were reduced neutrophils, leukocytes, and lymphocytes.

In the TROPiCS-02 study (locally advanced or metastatic HR-positive, HER2-negative breast cancer), the most common adverse reactions (incidence  $\geq$ 25%) were diarrhea, fatigue, nausea, alopecia, and constipation. The most frequent serious adverse reactions (SAR) (>1%) were diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%). SAR were reported in 28% of patients, and 6% discontinued therapy due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence  $\geq$ 25%) in the TROPiCS-02 study were reduced neutrophils and leukocytes.

#### **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 reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.

# Please see full Important Safety Information throughout, and click to see full <u>Prescribing Information</u>, including BOXED WARNING.

**References: 1.** TRODELVY. Prescribing Information. Gilead Sciences, Inc.; March 2025. **2.** Rugo HS, Bardia A, Marmé F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer. *J Clin Oncol.* 2022;40(29):3365-3376. doi:10.1200/JCO.22.01002 **3.** Bardia A, Hurvitz SA, Tolaney, SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med.* 2021;384(16):1529-1541. doi:10.1056/NEJMoa2028485 **4.** Immunomedics, Inc. Phase 3 study of sacituzumab govitecan (IMMU-132) versus treatment of physician's choice (TPC) in subjects with hormonal receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer (MBC) who have failed at least two prior chemotherapy regimens. Published December 21, 2018. Accessed April 22, 2025. https://ascopubs.org/doi/suppl/10.1200/JCO.22.01002/suppl\_file/protocol\_JCO.22.01002.pdf **5.** Immunomedics, Inc. An international multi-center, open-label, randomized, phase III trial of sacituzumab govitecan versus treatment of physician choice in patients with metastatic triple-negative breast cancer who received at least two prior treatments. Published November 18, 2015. Updated June 22, 2017. Accessed April 22, 2025. https://www.nejm.org/doi/suppl/10.1056/NEJMoa2028485/suppl\_file/nejmoa2028485\_protocol.pdf **6.** Rugo HS, Bardia A, Marme F, et al. Overall survival with sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomised, open-label, multicentre, phase 3 trial. *Lancet.* 2023;402(10411):1423-1433. doi:10.1016/S0I 40-6736(23)01245-X **7.** Rugo HS, Schmid P, Tolaney SM, et al. Health-related quality of life (HRQoL) in the phase 3 TROPiCS-02 trial of sacituzumab govitecan (SG) vs chemotherapy in HR+/HER2- metastatic breast cancer (mBC). Presented at: European Society for Medical Oncology Congress; September 9-13, 2022; Paris, France. Presentation 15530.



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