WARNING: NEUTROPENIA AND DIARRHEA
See full prescribing information for complete boxed warning.

Severe or life threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm³ 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. (5.1)

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. (2.3, 5.2)

---RECENT MAJOR CHANGES---
Indications and Usage (1) 04/2021
Dosage and Administration (2.4) 04/2021
Warnings and Precautions (5.1, 5.2, 5.3, 5.4, 5.5) 04/2021

---INDICATIONS AND USAGE---
TRODELVY 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. (1, 14)

---DOSAGE AND ADMINISTRATION---
- Do NOT substitute TRODELVY for or use with other drugs containing irinotecan or its active metabolite SN-38. (2.1)
- For intravenous infusion only. Do not administer as an intravenous push or bolus.
- The recommended dose is 10 mg/kg once weekly on Days 1 and 8 of continuous 21-day treatment cycles until disease progression or unacceptable toxicity. (2.2)
- Premedication for prevention of infusion reactions and prevention of chemotherapy-induced nausea and vomiting is recommended. (2.2)
- Monitor patients during the infusion and for at least 30 minutes after completion of infusion. Treatment interruption and/or dose reduction may be needed to manage adverse reactions. (2.2)

---ADVERSE REACTIONS---
Most common adverse reactions (incidence ≥25%) are nausea, neutropenia, diarrhea, fatigue, alopecia, anemia, vomiting, constipation, rash, decreased appetite, and abdominal pain. (6.1)

---DRUG INTERACTIONS---
- UGT1A1 inhibitors or inducers: Avoid concomitant use. (7)

---USE IN SPECIFIC POPULATIONS---
- Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2021
FULL PRESCRIBING INFORMATION: CONTENTS*

1  INDICATIONS AND USAGE
2  DOSAGE AND ADMINISTRATION
   2.1  Important Use Information
   2.2  Recommended Dose and Schedule
   2.3  Dose Modifications for Adverse Reactions
   2.4  Preparation for Administration
3  DOSAGE FORMS AND STRENGTHS
4  CONTRAINDICATIONS
5  WARNINGS AND PRECAUTIONS
   5.1  Neutropenia
   5.2  Diarrhea
   5.3  Hypersensitivity and Infusion Related Reactions
   5.4  Nausea and Vomiting
   5.5  Increased Risk of Adverse Reactions in Patients with Reduced
       UGT1A1 Activity
   5.6  Embryo-Fetal Toxicity
6  ADVERSE REACTIONS
   6.1  Clinical Trials Experience
   6.2  Immunogenicity
7  DRUG INTERACTIONS
   7.1  UGT1A1 Inhibitors or Inducers

8  USE IN SPECIFIC POPULATIONS
   8.1  Pregnancy
   8.2  Lactation
   8.3  Females and Males of Reproductive Potential
   8.4  Pediatric Use
   8.5  Geriatric Use
   8.6  Hepatic Impairment
9  OVERDOSAGE
10 DESCRIPTION
11 CLINICAL PHARMACOLOGY
   11.1  Mechanism of Action
   11.2  Pharmacodynamics
   11.3  Pharmacokinetics
   11.5  Pharmacogenomics
12 NONCLINICAL TOXICOLOGY
   12.1  Carcinogenesis, Mutagenesis, Impairment of Fertility
13 CLINICAL STUDIES
14 REFERENCES
15 HOW SUPPLIED/STORAGE AND HANDLING
16 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.
WARNING: NEUTROPENIA AND DIARRHEA

- Severe or life threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm³ or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patient with febrile neutropenia without delay [see Warnings and Precautions (5.1)].

- 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 [see Warnings and Precautions (5.2)]. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤ Grade 1 and reduce subsequent doses [see Dosage and Administration (2.3)].

1 INDICATIONS AND USAGE

TRODELVY is 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.

2 DOSAGE AND ADMINISTRATION

2.1 Important Use Information

Do NOT substitute TRODELVY for or use with other drugs containing irinotecan or its active metabolite SN-38.

2.2 Recommended Dose and Schedule

The recommended dose of TRODELVY is 10 mg/kg administered as an intravenous infusion once weekly on Days 1 and 8 of 21-day treatment cycles. Continue treatment until disease progression or unacceptable toxicity. Do not administer TRODELVY at doses greater than 10 mg/kg.

Administer TRODELVY as an intravenous infusion only. Do not administer as an intravenous push or bolus.

First infusion: Administer infusion over 3 hours. Observe patients during the infusion and for at least 30 minutes following the initial dose, for signs or symptoms of infusion-related reactions [see Warning and Precautions (5.3)].

Subsequent infusions: Administer infusion over 1 to 2 hours if prior infusions were tolerated. Observe patients during the infusion and for at least 30 minutes after infusion.

Premedication

Prior to each dose of TRODELVY, premedication for prevention of infusion reactions and prevention of chemotherapy-induced nausea and vomiting (CINV) is recommended.

- Premedicate with antipyretics, H1 and H2 blockers prior to infusion, and corticosteroids may be used for patients who had prior infusion reactions.

- 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).
2.3 Dose Modifications for Adverse Reactions

Infusion-related Reactions

Slow or interrupt the infusion rate of TRODELVY if the patient develops an infusion-related reaction. Permanently discontinue TRODELVY for life-threatening infusion-related reactions [see Warnings and Precautions (5.3)]

Dose Modifications for Adverse Reactions

Withhold or discontinue TRODELVY to manage adverse reactions as described in Table 1. Do not re-escalate the TRODELVY dose after a dose reduction for adverse reactions has been made.

Table 1: Dose Modifications for Adverse Reactions

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Occurrence</th>
<th>Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severe Neutropenia</strong> [see Warnings and Precautions (5.1)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 4 neutropenia ≥7 days, OR Grade 3 febrile neutropenia (absolute neutrophil count &lt;1000/mm³ and fever ≥38.5°C), OR At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing by 2 or 3 weeks for recovery to ≤Grade 1</td>
<td>First</td>
<td>25% dose reduction and administer granulocyte-colony stimulating factor (G-CSF)</td>
</tr>
<tr>
<td>At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing beyond 3 weeks for recovery to ≤Grade 1</td>
<td>Second</td>
<td>50% dose reduction</td>
</tr>
<tr>
<td></td>
<td>Third</td>
<td>Discontinue treatment</td>
</tr>
<tr>
<td><strong>Severe Non-Neutropenic Toxicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 4 non-hematologic toxicity of any duration, OR Any Grade 3-4 nausea, vomiting or diarrhea due to treatment that is not controlled with antiemetics and anti-diarrheal agents [see Warnings and Precautions (5.2, 5.4)], OR Other Grade 3-4 non-hematologic toxicity persisting &gt;48 hours despite optimal medical management, OR At time of scheduled treatment, Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which delays dose by 2 or 3 weeks for recovery to ≤Grade 1</td>
<td>First</td>
<td>25% dose reduction</td>
</tr>
<tr>
<td>In the event of Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which does not recover to ≤Grade 1 within 3 weeks</td>
<td>Second</td>
<td>50% dose reduction</td>
</tr>
<tr>
<td></td>
<td>Third</td>
<td>Discontinue treatment</td>
</tr>
</tbody>
</table>

2.4 Preparation for Administration

Reconstitution
- TRODELVY is a cytotoxic drug.
- Follow applicable special handling and disposal procedures\(^1\).
Calculate the required dose (mg) of TRODELVY based on the patient’s body weight at the beginning of each treatment cycle (or more frequently if the patient’s body weight changed by more than 10% since the previous administration) [see Dosage and Administration (2.2)].

Allow the required number of vials to warm to room temperature.

Using a sterile syringe, slowly inject 20 mL of 0.9% Sodium Chloride Injection, USP, into each 180 mg TRODELVY vial. The resulting concentration will be 10 mg/mL.

Gently swirl vials and allow to dissolve for up to 15 minutes. Do not shake. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The solution should be free of visible particulates, clear and yellow. Do not use the reconstituted solution if it is cloudy or discolored.

Use immediately to prepare a diluted TRODELVY infusion solution.

Dilution

- Calculate the required volume of the reconstituted TRODELVY solution needed to obtain the appropriate dose according to patient’s body weight. Withdraw this amount from the vial(s) using a syringe. Discard any unused portion remaining in the vial(s).
- Adjust the volume in the infusion bag as needed with 0.9% Sodium Chloride Injection, USP, to obtain a concentration of 1.1 mg/mL to 3.4 mg/mL (total volume should not exceed 500 mL). For patients whose body weight exceeds 170 kg, divide the total dosage of TRODELVY equally between two 500 mL infusion bags and infuse sequentially via slow infusion.
- Slowly inject the required volume of reconstituted TRODELVY solution into a polyvinyl chloride, polypropylene or ethylene/propylene copolymer infusion bag, to minimize foaming. Do not shake the contents.
- Only 0.9% Sodium Chloride Injection, USP, should be used since the stability of the reconstituted product has not been determined with other infusion-based solutions. Use the diluted solution in the infusion bag immediately. If not used immediately, the infusion bag containing TRODELVY solution can be stored refrigerated 2°C to 8°C (36°F to 46°F) for up to 4 hours. After refrigeration, administer diluted solution within 4 hours (including infusion time).

Do Not Freeze or Shake. Protect from Light.

Administration

- Administer TRODELVY as an intravenous infusion. Protect infusion bag from light.
- An infusion pump may be used.
- Do not mix TRODELVY, or administer as an infusion, with other medicinal products.
- Upon completion of the infusion, flush the intravenous line with 20 mL 0.9% Sodium Chloride Injection, USP.

3 DOSAGE FORMS AND STRENGTHS

For injection: 180 mg off-white to yellowish lyophilized powder in a single-dose vial.

4 CONTRAINDICATIONS

TRODELVY is contraindicated in patients who have experienced a severe hypersensitivity reaction to TRODELVY [see Warnings and Precautions (5.3)].

5 WARNINGS AND PRECAUTIONS

5.1 Neutropenia

TRODELVY can cause severe or life-threatening neutropenia that may result in death. Neutropenia occurred in 62% of patients treated with TRODELVY, leading to permanent discontinuation of TRODELVY in 0.5% of patients. Grade 3-4 neutropenia occurred in 47% of patients. Febrile neutropenia occurred in 6% of patients.
Withhold TRODELVY for absolute neutrophil count below 1500/mm³ on Day 1 of any cycle or neutrophil count below 1000/mm³ on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Dose modifications may be required due to neutropenia. [see Dosage and Administration (2.3)].

5.2 Diarrhea
TRODELVY can cause severe diarrhea. Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3 diarrhea occurred in 12% of all patients treated with TRODELVY. Neutropenic colitis occurred in 0.5% of patients.

Withhold TRODELVY for Grade 3-4 diarrhea at the time of scheduled treatment administration and resume when resolved to ≤Grade 1 [see Dosage and Administration (2.3)].

At the onset of diarrhea, 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 with TRODELVY (e.g., abdominal cramping, diarrhea, salivation, etc.) can receive appropriate premedication (e.g., atropine) for subsequent treatments.

5.3 Hypersensitivity and Infusion-Related Reactions
TRODELVY can cause severe and life-threatening hypersensitivity. Anaphylactic reactions have been observed in clinical trials with TRODELVY [see Contraindications (4)].

Hypersensitivity reactions within 24 hours of dosing occurred in 37% of patients treated with TRODELVY. Grade 3-4 hypersensitivity occurred in 1% of patients treated with TRODELVY. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.4%.

Pre-infusion medication for patients receiving TRODELVY is recommended. Observe patients closely for hypersensitivity and infusion-related reactions during each TRODELVY infusion and for at least 30 minutes after completion of each infusion [see Dosage and Administration (2.3)]. Medication to treat such reactions, as well as emergency equipment, should be available for immediate use.

5.4 Nausea and Vomiting
TRODELVY is emetogenic. Nausea occurred in 67% of all patients treated with TRODELVY. Grade 3-4 nausea occurred in 5% of patients.

Vomiting occurred 40% of all patients treated with TRODELVY. 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 at the time of scheduled treatment administration and resume with additional supportive measures when resolved to ≤Grade 1 [see Dosage and Administration (2.3)].
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.

5.5 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 when treated with TRODELVY.

The incidence of neutropenia and anemia was analyzed in 577 patients who received TRODELVY and had UGT1A1 genotype results. In patients homozygous for the UGT1A1 *28 allele (n=70), the incidence of Grade 3-4 neutropenia was 69%. In patients heterozygous for the UGT1A1*28 allele (n=246), the incidence of Grade 3-4 neutropenia was 48%. In patients homozygous for the wild-type allele (n=261), the incidence of Grade 3-4 neutropenia was 46% [see Clinical Pharmacology (12.5)]. In patients homozygous for the UGT1A1*28 allele (n=70), the incidence of Grade 3-4 anemia was 24%. In patients heterozygous for the UGT1A1*28 allele (n=246), the incidence of Grade 3-4 anemia was 8%. In patients homozygous for the wild-type allele (n=261), the incidence of Grade 3-4 anemia was 10%.

Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY based on severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate UGT1A1 reduced function [see Dosage and Administration (2.3)].

5.6 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 [see Clinical Pharmacology (12.1) and Nonclinical Toxicology (13.1)]. 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 [see Use in Specific Populations (8.1, 8.3)].

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

- Neutropenia [see Warnings and Precautions (5.1)]
- Diarrhea [see Warnings and Precautions (5.2)]
- Hypersensitivity and Infusion-Related Reactions [see Warnings and Precautions (5.3)]
- Nausea and Vomiting [see Warnings and Precautions (5.4)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The pooled safety population described in the Warnings and Precautions section reflect exposure to TRODELVY as a single agent in 660 patients from two studies, IMMU-132-01 and IMMU-132-05 which included 366 patients with mTNBC who had received prior systemic chemotherapy for advanced disease. TRODELVY was administered as an intravenous infusion once weekly on Days 1 and 8 of 21-day treatment cycles at doses of 10 mg/kg until disease progression or unacceptable toxicity. Among the 660 patients treated with TRODELVY, the median duration of treatment was 4.1 months (range: 0 to 51 months). In this pooled safety population, the most common (≥ 25%) adverse reactions
were nausea, neutropenia, diarrhea, fatigue, alopecia, anemia, vomiting, constipation, rash, decreased appetite and abdominal pain.

**ASCENT Study**

The safety of TRODELVY was evaluated in a randomized, active-controlled, open-label trial (ASCENT) in patients with mTNBC who had previously received a taxane and at least two prior therapies. Patients were randomized (1:1) to receive either TRODELVY (n=258) or single agent chemotherapy (n=224) and were treated until disease progression or unacceptable toxicity [see Clinical Studies (14)]. For patients treated with TRODELVY, the median duration of treatment was 4.4 months (range: 0 to 23 months).

Serious adverse reactions occurred in 27% of patients receiving TRODELVY. Serious adverse reactions in >1% of patients receiving TRODELVY included neutropenia (7%), diarrhea (4%), and pneumonia (3%). Fatal adverse reactions occurred in 1.2% of patients who received TRODELVY, including respiratory failure (0.8%) and pneumonia (0.4%). TRODELVY was permanently discontinued for adverse reactions in 5% of patients. Adverse reactions leading to permanent discontinuation in ≥1% of patients who received TRODELVY were pneumonia (1%) and fatigue (1%).

Adverse reactions leading to a treatment interruption of TRODELVY occurred in 63% of patients. The most frequent (≥5%) adverse reactions leading to a treatment interruption were neutropenia (47%), diarrhea (5%), respiratory infection (5%), and leukopenia (5%).

Adverse reactions leading to a dose reduction of TRODELVY occurred in 22% of patients. The most frequent (>4%) adverse reactions leading to a dose reduction were neutropenia (11%) and diarrhea (5%).

Granulocyte-colony stimulating factor (G-CSF) was used in 44% of patients who received TRODELVY.

Tables 2 and 3 summarize adverse reactions and select laboratory abnormalities, respectively, in the ASCENT study.
<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TRODELVY (n=258)</th>
<th>Single Agent Chemotherapy (n=224)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades %</td>
<td>Grade 3 - 4 %</td>
</tr>
<tr>
<td><strong>Blood and lymphatic system disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia(^{i})</td>
<td>64</td>
<td>52</td>
</tr>
<tr>
<td>Anemia(^{ii})</td>
<td>40</td>
<td>9</td>
</tr>
<tr>
<td>Leukopenia(^{iii})</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Lymphopenia(^{iv})</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>59</td>
<td>11</td>
</tr>
<tr>
<td>Nausea</td>
<td>57</td>
<td>3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>33</td>
<td>2</td>
</tr>
<tr>
<td>Constipation</td>
<td>37</td>
<td>0.4</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>Stomatitis(^{v})</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td><strong>General disorders and administration site conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue(^{vi})</td>
<td>65</td>
<td>6</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>15</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Infections and infestation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>13</td>
<td>0.4</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td><strong>Investigations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase increased</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td><strong>Metabolism and nutrition disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>28</td>
<td>2</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Hypomagnesaemia</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>12</td>
<td>0.4</td>
</tr>
<tr>
<td><strong>Nervous system disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>18</td>
<td>0.8</td>
</tr>
<tr>
<td>Dizziness</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td><strong>Psychiatric disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td><strong>Respiratory, thoracic and mediastinal disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td><strong>Skin and subcutaneous tissue disorders</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Study IMMU-132-01
The safety of TRODELVY was evaluated in a single-arm, open-label study (IMMU-132-01) in patients with mTNBC and other malignancies, which included 108 patients with mTNBC who had received at least two prior treatments for metastatic disease [see Clinical Studies (14)]. TRODELVY was administered as an intravenous infusion once weekly on Days 1 and 8 of 21-day treatment cycles at doses up to 10 mg/kg until disease progression or unacceptable toxicity. The median treatment duration in these 108 patients was 5.1 months (range: 0–51 months).

Serious adverse reactions occurred in 31% of the patients. Serious adverse reactions in >1% of patients receiving TRODELVY included febrile neutropenia (6%), vomiting (5%), nausea (3%), dyspnea (3%), diarrhea (4%), anemia (2%), pleural effusion, neutropenia, pneumonia, dehydration (each 2%).

TRODELVY was permanently discontinued for adverse reactions in 2% of patients. Adverse reactions leading to permanent discontinuation were anaphylaxis, anorexia/fatigue, headache (each 0.9%). Forty-five percent (45%) of patients experienced an adverse reaction leading to treatment interruption. The most common adverse reaction leading to treatment interruption was neutropenia (33%). Adverse reactions leading to dose reduction occurred in 33% of patients treated with TRODELVY, with 24% having one dose reduction, and 9% with two dose reductions. The most common adverse reaction leading to dose reductions was neutropenia/febrile neutropenia.

Adverse reactions occurring in ≥10% of patients with mTNBC in the IMMU-132-01 study are summarized in Table 2.
Table 4: Adverse Reactions in ≥ 10% of Patients with mTNBC in IMMU-132-01

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TRODELYV (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1-4 (%)</td>
</tr>
<tr>
<td>Any adverse reaction</td>
<td>100</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>69</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>63</td>
</tr>
<tr>
<td>Vomiting</td>
<td>49</td>
</tr>
<tr>
<td>Constipation</td>
<td>34</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>26</td>
</tr>
<tr>
<td>Mucositis</td>
<td>14</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>77</td>
</tr>
<tr>
<td>Fatigue</td>
<td>57</td>
</tr>
<tr>
<td>Edema</td>
<td>19</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>14</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>74</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>64</td>
</tr>
<tr>
<td>Anemia</td>
<td>52</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>14</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>68</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>30</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>24</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>21</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>19</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>16</td>
</tr>
<tr>
<td>Dehydration</td>
<td>13</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>63</td>
</tr>
<tr>
<td>Alopecia</td>
<td>38</td>
</tr>
<tr>
<td>Rash</td>
<td>31</td>
</tr>
<tr>
<td>Pruritus</td>
<td>17</td>
</tr>
<tr>
<td>Dry Skin</td>
<td>15</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>56</td>
</tr>
<tr>
<td>Headache</td>
<td>23</td>
</tr>
<tr>
<td>Dizziness</td>
<td>22</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>24</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>11</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>55</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>21</td>
</tr>
</tbody>
</table>

Reference ID: 4775161
Table 4: Adverse Reactions in ≥ 10% of Patients with mTNBC in IMMU-132-01

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TRODELVY (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1-4 (%)</td>
</tr>
<tr>
<td>Respiratory Infection\textsuperscript{vii}</td>
<td>26</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>54</td>
</tr>
<tr>
<td>Back pain</td>
<td>23</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>17</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>11</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>54</td>
</tr>
<tr>
<td>Cough\textsuperscript{viii}</td>
<td>22</td>
</tr>
<tr>
<td>Dyspnea\textsuperscript{ix}</td>
<td>21</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>26</td>
</tr>
<tr>
<td>Insomnia</td>
<td>13</td>
</tr>
</tbody>
</table>

Graded per NCI CTCAE v. 4.0
\textsuperscript{i} Including abdominal pain, distention, pain (upper), discomfort, tenderness.
\textsuperscript{ii} Including stomatitis, esophagitis, and mucosal inflammation
\textsuperscript{iii} Including fatigue and asthenia.
\textsuperscript{iv} Including edema; and peripheral, localized, and periorbital edema
\textsuperscript{v} Including rash; maculopapular, erythematous, generalized rash; dermatitis acneiform; skin disorder, irritation, and exfoliation
\textsuperscript{vi} Including gait disturbance, hypoesthesia, muscular weakness, paresthesia, peripheral and sensory neuropathy
\textsuperscript{vii} Including lower and upper respiratory tract infection, pneumonia, influenza, viral upper respiratory infection, bronchitis and respiratory syncytial virus infection
\textsuperscript{viii} Includes cough and productive cough
\textsuperscript{ix} Includes dyspnea and exertional dyspnea

Table 5: Laboratory Abnormalities observed in ≥10% of Patients while receiving TRODELVY

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>TRODELVY (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
</tr>
<tr>
<td>Decreased hemoglobin</td>
<td>93</td>
</tr>
<tr>
<td>Decreased leukocytes</td>
<td>91</td>
</tr>
<tr>
<td>Decreased neutrophils</td>
<td>82</td>
</tr>
<tr>
<td>Increased activated partial thromboplastin time</td>
<td>60</td>
</tr>
<tr>
<td>Decreased platelets</td>
<td>30</td>
</tr>
<tr>
<td>Chemistry</td>
<td></td>
</tr>
<tr>
<td>Increased alkaline phosphatase</td>
<td>57</td>
</tr>
<tr>
<td>Decreased magnesium</td>
<td>51</td>
</tr>
</tbody>
</table>

Reference ID: 4775161
### Laboratory Abnormality

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>TRODELVY (n=108)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grade 3-4 (%)</td>
</tr>
<tr>
<td>Decreased calcium</td>
<td>49</td>
<td>3</td>
</tr>
<tr>
<td>Increased glucose</td>
<td>48</td>
<td>3</td>
</tr>
<tr>
<td>Increased aspartate aminotransferase</td>
<td>45</td>
<td>3</td>
</tr>
<tr>
<td>Decreased albumin</td>
<td>39</td>
<td>1</td>
</tr>
<tr>
<td>Increased alanine aminotransferase</td>
<td>35</td>
<td>2</td>
</tr>
<tr>
<td>Decreased potassium</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>Decreased phosphate</td>
<td>29</td>
<td>5</td>
</tr>
<tr>
<td>Decreased sodium</td>
<td>25</td>
<td>4.7</td>
</tr>
<tr>
<td>Increased magnesium</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>Decreased glucose</td>
<td>19</td>
<td>2</td>
</tr>
</tbody>
</table>

### 6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other sacituzumab govitecan products may be misleading.

The analysis of immunogenicity of TRODELVY in serum samples from 106 patients with mTNBC was evaluated using an electrochemiluminescence (ECL)-based immunoassay to test for anti-sacituzumab govitecan-hziy antibodies. Detection of the anti-sacituzumab govitecan-hziy antibodies was done using a 3-tier approach: screen, confirm, and titer. Persistent anti-sacituzumab govitecan-hziy antibodies developed in 2% (2/106) of patients.

### 7 DRUG INTERACTIONS

#### 7.1 Effect of Other Drugs on TRODELVY

**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 [see Warning and Precaution (5.5) and Clinical Pharmacology (12.3, 12.5)]. Avoid administering UGT1A1 inhibitors with TRODELVY.

**UGT1A1 Inducers**

Exposure to SN-38 may be substantially reduced in patients concomitantly receiving UGT1A1 enzyme inducers [see Warning and Precaution (5.5) and Clinical Pharmacology (12.3, 12.5)]. Avoid administering UGT1A1 inducers with TRODELVY.
8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. TRODELVY contains a genotoxic component, SN-38, and is toxic to rapidly dividing cells [see Clinical Pharmacology (12.1) and Nonclinical Toxicology (13.1)]. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 – 4% and 15 – 20%, respectively.

Data

Animal data
There were no reproductive and developmental toxicology studies conducted with sacituzumab govitecan-hziy.

8.2 Lactation

Risk Summary
There is no information regarding the presence of sacituzumab govitecan-hziy or SN-38 in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment and for 1 month after the last dose of TRODELVY.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing
Verify the pregnancy status of females of reproductive potential prior to the initiation of TRODELVY.

Contraception

Females
TRODELVY can cause fetal harm when administered to a pregnant woman [see Use in Specific Populations (8.1)]. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose.

Males
Because of the potential for genotoxicity, 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.

Infertility

Females
Based on findings in animals, TRODELVY may impair fertility in females of reproductive potential [see Nonclinical Toxicology (13.1)].

8.4 Pediatric Use
Safety and effectiveness of TRODELVY have not been established in pediatric patients.
8.5 Geriatric Use
Of the patients who received TRODELVY, 28% of all patients were ≥65 years old. No overall differences in safety and effectiveness were observed between these patients and younger patients.

8.6 Hepatic Impairment
No adjustment to the starting dose is required when administering TRODELVY to patients with mild hepatic impairment (bilirubin ≤1.5 ULN and AST/ALT <3 ULN).

The exposure of TRODELVY in patients with mild hepatic impairment (bilirubin ≤ULN and AST >ULN, or bilirubin >1.0 to 1.5 ULN and AST of any level; n=59 was similar to patients with normal hepatic function (bilirubin or AST <ULN; n=191).

The safety of TRODELVY in patients with moderate or severe hepatic impairment has not been established. TRODELVY has not been tested in patients with serum bilirubin > 1.5 ULN, or AST and ALT > 3 ULN, or AST and ALT > 5 ULN and associated with liver metastases.

No dedicated trial was performed to investigate the tolerability of TRODELVY in patients with moderate or severe hepatic impairment. No recommendations can be made for the starting dose in these patients.

10 OVERDOSAGE
In a clinical trial, planned doses of up to 18 mg/kg (approximately 1.8 times the maximum recommended dose of 10 mg/kg) of TRODELVY were administered. In these patients, a higher incidence of severe neutropenia was observed.

11 DESCRIPTION
Sacituzumab govitecan-hziy is a Trop-2 directed antibody and topoisomerase inhibitor conjugate, composed of the following three components:

- the humanized monoclonal antibody, hRS7 IgG1κ (also called sacituzumab), which binds to Trop-2 (the trophoblast cell-surface antigen-2);
- the drug SN-38, a topoisomerase inhibitor;
- a hydrolysable linker (called CL2A), which links the humanized monoclonal antibody to SN-38.

The recombinant monoclonal antibody is produced by mammalian (murine myeloma) cells, while the small molecule components SN-38 and CL2A are produced by chemical synthesis. Sacituzumab govitecan-hziy contains on average 7 to 8 molecules of SN-38 per antibody molecule. Sacituzumab govitecan-hziy has a molecular weight of approximately 160 kilodaltons. Sacituzumab govitecan-hziy has the following chemical structure.
TRODELVY (sacituzumab govitecan-hziy) for injection is a sterile, preservative-free, off-white to yellowish lyophilized powder for intravenous use in a 50 mL clear glass single-dose vial, with a rubber stopper and crimp-sealed with an aluminum flip-off cap.

Each single-dose vial of TRODELVY delivers 180 mg sacituzumab govitecan-hziy, 77.3 mg 2-(N-morpholino) ethane sulfonic acid (MES), 1.8 mg polysorbate 80, and 154 mg trehalose dihydrate. Reconstitution with 20 mL of 0.9% Sodium Chloride Injection, USP, results in a concentration of 10 mg/mL with a pH of 6.5.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Sacituzumab govitecan-hziy is a Trop-2-directed antibody-drug conjugate. Sacituzumab is a humanized antibody that recognizes Trop-2. The small molecule, SN-38, is a topoisomerase I inhibitor, which is covalently attached to the antibody by a linker. Pharmacology data suggest that sacituzumab govitecan-hziy binds to Trop-2-expressing cancer cells and is internalized with the subsequent release of SN-38 via hydrolysis of the linker. SN-38 interacts with topoisomerase I and prevents re-ligation of topoisomerase I-induced single strand breaks. The resulting DNA damage leads to apoptosis and cell death. Sacituzumab govitecan-hziy decreased tumor growth in mouse xenograft models of triple-negative breast cancer.

12.2 Pharmacodynamics
The TRODELVY exposure-response relationships and pharmacodynamic time-course for efficacy have not been fully characterized.

Cardiac electrophysiology
The maximum mean change from baseline was 9.7 msec (the upper bound of the two-sided 90% confidence interval is 16.8 msec) at the recommended dose. A positive exposure-response relationship was observed between QTc increases and SN-38 concentrations.
12.3 Pharmacokinetics

The serum pharmacokinetics of sacituzumab govitecan-hziy and SN-38 were evaluated in study IMMU132-05 in a population of mTNBC patients who received sacituzumab govitecan-hziy as a single agent at a dose of 10 mg/kg. The pharmacokinetic parameters of sacituzumab govitecan-hziy and free SN-38 are presented in Table 6.

Table 6: Summary of Mean PK Parameters (CV%) of Sacituzumab Govitecan-hziy and Free SN-38

<table>
<thead>
<tr>
<th></th>
<th>Sacituzumab govitecan-hziy</th>
<th>Free SN-38</th>
</tr>
</thead>
<tbody>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; [ng/mL]</td>
<td>240000 (22.2%)</td>
<td>90.6 (65.0%)</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-168&lt;/sub&gt; [ng*h/mL]</td>
<td>5340000 (23.7%)</td>
<td>2730 (41.1%)</td>
</tr>
</tbody>
</table>

C<sub>max</sub>: maximum plasma concentration
AUC<sub>0-168</sub>: area under plasma concentration curve through 168 hours

Distribution

Based on population pharmacokinetic analysis, the central volume distribution of sacituzumab govitecan-hziy is 2.96 L.

Elimination

The mean half-life of sacituzumab govitecan-hziy and free SN-38 is 15.3 and 19.7 hours, respectively. Based on population pharmacokinetic analysis, the clearance of the sacituzumab govitecan-hziy is 0.14 L/h.

Metabolism

No metabolism studies with sacituzumab govitecan-hziy have been conducted. SN-38 (the small molecule moiety of sacituzumab govitecan-hziy) is metabolized via UGT1A1. The glucuronide metabolite of SN-38 (SN-38G) was detectable in the serum of patients.

Specific Populations

Pharmacokinetic analyses in patients treated with TRODELVY (n=527) did not identify an effect of age, race, or mild renal impairment on the pharmacokinetics of sacituzumab govitecan-hziy. Renal elimination is known to contribute minimally to the excretion of SN-38, the small molecule moiety of sacituzumab govitecan-hziy. There are no data on the pharmacokinetics of sacituzumab govitecan-hziy in patients with moderate renal impairment or end-stage renal disease (CLcr ≤30 mL/min).

The exposure of sacituzumab govitecan-hziy is similar in patients with mild hepatic impairment (bilirubin ≤ULN and AST >ULN, or bilirubin >1.0 to <1.5 ULN and AST of any level; n=59) to patients with normal hepatic function (bilirubin or AST <ULN; n=191).

Sacituzumab govitecan-hziy exposure is unknown in patients with moderate or severe hepatic impairment. SN-38 exposure may be elevated in such patients due to decreased hepatic UGT1A1 activity.

Drug Interaction Studies

No drug-drug interaction studies were conducted with sacituzumab govitecan-hziy or its components. Inhibitors or inducers of UGT1A1 are expected to increase or decrease SN-38 exposure, respectively [see Drug Interactions (7)].

12.5 Pharmacogenomics

SN-38 is metabolized via UGT1A1 [see Clinical Pharmacology (12.3)]. Genetic variants of the UGT1A1 gene such as the UGT1A1*28 allele lead to reduced UGT1A1 enzyme activity. Individuals who are homozygous for the UGT1A1*28
allele are at increased risk for neutropenia, febrile neutropenia, and anemia from TRODELVY [see Warnings and Precautions (5.5)]. Approximately 20% of the Black or African American population, 10% of the White population, and 2% of the East Asian population are homozygous for the UGT1A1*28 allele. Decreased function alleles other than UGT1A1*28 may be present in certain populations.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenicity studies have not been conducted with sacituzumab govitecan-hziy.

SN-38 was clastogenic in an in vitro mammalian cell micronucleus test in Chinese hamster ovary cells and was not mutagenic in an in vitro bacterial reverse mutation (Ames) assay.

Fertility studies with sacituzumab govitecan-hziy have not been conducted. In a repeat-dose toxicity study in cynomolgus monkeys, intravenous administration of sacituzumab govitecan-hziy on Day 1 and Day 4 resulted in endometrial atrophy, uterine hemorrhage, increased follicular atresia of the ovary, and atrophy of vaginal epithelial cells at doses ≥60 mg/kg (≥6 times the human recommended dose of 10 mg/kg based on body weight).

14 CLINICAL STUDIES
ASCENT
Efficacy was evaluated in a multicenter, open-label, randomized study (ASCENT; NCT02574455) conducted in 529 patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who had relapsed after at least two prior chemotherapies for breast cancer (one of which could be in the neoadjuvant or adjuvant setting provided progression occurred within a 12 month period). All patients received previous taxane treatment in either the adjuvant, neoadjuvant, or advanced stage unless there was a contraindication or intolerance to taxanes during or at the end of the first taxane cycle. Magnetic resonance imaging (MRI) to determine brain metastases was required prior to enrollment for patients with known or suspected brain metastases. Patients with brain metastases were allowed to enroll up to a pre-defined maximum of 15% of patients in the ASCENT trial. Patients with known Gilbert’s disease or bone-only disease were excluded.

Patients were randomized (1:1) to receive TRODELVY 10 mg/kg as an intravenous infusion on Days 1 and 8 of a 21-day (n=267) or physician’s choice of single agent chemotherapy (n=262). Single agent chemotherapy was determined by the investigator before randomization from one of the following choices: eribulin (n=139), capecitabine (n=33), gemcitabine (n=38), or vinorelbine (n=52).

Patients were treated until disease progression or unacceptable toxicity. The major efficacy outcome was progression-free survival (PFS) in patients without brain metastases at baseline (i.e., BMNeg) as measured by a blinded, independent, centralized review assessed using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria. Additional efficacy measures included PFS for the full population (all patients with and without brain metastases) and overall survival (OS).

The median age of patients in the full population (n = 529) was 54 years (range: 27–82 years); 99.6% were female; 79% were White, 12% were Black/African American; and 81% of patients were < 65 years of age. All patients had an ECOG performance status of 0 (43%) or 1 (57%). Forty-two percent of patients had hepatic metastases, 9% were BRCA1/BRCA2 mutational status positive, and 70% were TNBC at diagnosis. Twelve percent had baseline brain metastases previously treated and stable (n=61; 32 on TRODELVY arm and 29 on single agent chemotherapy arm).
Overall, 29% of patients had received prior PD-1/PD-L1 therapy. Thirteen percent of patients in the TRODELVY group in the full population received only 1 prior line of systemic therapy in the metastatic setting.

The efficacy results are summarized in Table 7 and are shown in Figure 1 and Figure 2. Efficacy results for the subgroup of patients who had received only 1 prior line of systemic therapy in the metastatic setting (in addition to having disease recurrence or progression within 12 months of neoadjuvant/adjuvant systemic therapy) were consistent with those who had received at least two prior lines in the metastatic setting.

### Table 7: Efficacy Results from ASCENT

<table>
<thead>
<tr>
<th></th>
<th>All Randomized Patients</th>
<th>TRODELVY n=267</th>
<th>Single Agent Chemotherapy n=262</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Progression-Free Survival(^1) per BICR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease Progression or Death (%)</td>
<td>190 (71%)</td>
<td>171 (65%)</td>
<td></td>
</tr>
<tr>
<td>Median PFS in months (95% CI)</td>
<td>4.8 (4.1, 5.8)</td>
<td>1.7 (1.5, 2.5)</td>
<td></td>
</tr>
<tr>
<td>Hazard ratio(^2) (95% CI)</td>
<td>0.43 (0.35, 0.54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Overall Survival</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths (%)</td>
<td>179 (67%)</td>
<td>206 (79%)</td>
<td></td>
</tr>
<tr>
<td>Median OS in months (95% CI)</td>
<td>11.8 (10.5, 13.8)</td>
<td>6.9 (5.9, 7.6)</td>
<td></td>
</tr>
<tr>
<td>Hazard ratio(^2) (95% CI)</td>
<td>0.51 (0.41, 0.62)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^1\)PFS is defined as the time from the date of randomization to the date of the first radiological disease progression or death due to any cause, whichever comes first.

\(^2\)Stratified log-rank test adjusted for stratification factors: number of prior chemotherapies, presence of known brain metastases at study entry, and region.

CI = Confidence Interval
An exploratory analysis of PFS in patients with previously treated, stable brain metastases showed a stratified HR of 0.65 (95% CI: 0.35, 1.22). The median PFS in the TRODELVY arm was 2.8 months (95% CI: 1.5, 3.9) and the median PFS with single agent chemotherapy was 1.6 months (95% CI: 1.3, 2.9). Exploratory OS analysis in the same population showed a stratified HR of 0.87 (95% CI: 0.47, 1.63). The median OS in the TRODELVY arm was 6.8 months (95% CI: 4.7, 14.1) and the median OS with single agent chemotherapy was 7.4 months (95% CI: 4.7, 11.1).
IMMU-132-01 (NCT01631552)

The efficacy of TRODELVY was evaluated in a multicenter, single-arm, trial that enrolled 108 patients with metastatic triple-negative breast cancer (mTNBC) who had received at least two prior treatments for metastatic disease. Patients with bulky disease, defined as a mass >7 cm, were not eligible. Patients with treated brain metastases not receiving high dose steroids (>20 mg prednisone or equivalent) for at least four weeks were eligible. Patients with known Gilbert’s disease were excluded.

Patients received TRODELVY 10 mg/kg intravenously on Days 1 and 8 of a 21-day treatment cycle. Patients were treated with TRODELVY until disease progression or intolerance to the therapy. Tumor imaging was obtained every 8 weeks, with confirmatory CT/MRI scans obtained 4-6 weeks after an initial partial or complete response, until progression requiring treatment discontinuation. Major efficacy outcome measures were investigator assessed overall response rate (ORR) using RECIST 1.1 and duration of response.

The median age was 55 years (range: 31 – 80 years); 87% of patients were younger than 65 years. The majority of patients were female (99%) and White (76%). At study entry, all patients had an ECOG performance status of 0 (29%) or 1 (71%). Seventy-six percent had visceral disease, 42% had hepatic metastases, 56% had lung/pleura metastases, and 2% had brain metastases. Twelve patients (11%) had Stage IV disease at the time of initial diagnosis.

The median number of prior systemic therapies received in the metastatic setting was 3 (range: 2 - 10). Prior chemotherapies in the metastatic setting included carboplatin or cisplatin (69%), gemcitabine (55%), paclitaxel or docetaxel (53%), capecitabine (51%), eribulin (45%), doxorubicin (24%), vinorelbine (16%), cyclophosphamide (19%), and ixabepilone (8%).

Overall, 98% of patients had received prior taxanes and 86% had received prior anthracyclines either in the (neo)adjuvant or metastatic setting.

Table 8 summarizes the efficacy results.

Table 8: Efficacy results for patients with mTNBC in IMMU-132-01

<table>
<thead>
<tr>
<th>TRODELVY (N=108)</th>
<th>Overall Response Rate i</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR (95% CI)</td>
<td>33.3% (24.6, 43.1)</td>
</tr>
<tr>
<td>Complete response</td>
<td>2.8%</td>
</tr>
<tr>
<td>Partial response</td>
<td>30.6%</td>
</tr>
</tbody>
</table>

Response duration i

<table>
<thead>
<tr>
<th>Number of responders</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median, Months (95% CI)</td>
<td>7.7 (4.9, 10.8)</td>
</tr>
<tr>
<td>Range, Months</td>
<td>1.9+, 30.4+</td>
</tr>
<tr>
<td>% with duration ≥6 months</td>
<td>55.6%</td>
</tr>
<tr>
<td>% with duration ≥12 months</td>
<td>16.7%</td>
</tr>
</tbody>
</table>

i investigator assessment
CI: confidence interval
+: denotes ongoing

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING
TRODELVY (sacituzumab govitecan-hziy) for injection is a sterile, off-white to yellowish lyophilized powder in a single-dose vial. Each TRODELVY vial is individually boxed in a carton:
- NDC 55135-132-01 contains one 180 mg vial

Store vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light until time of reconstitution. Do not freeze.

TRODELVY is a cytotoxic drug. Follow applicable special handling and disposal procedures.

17 PATIENT COUNSELING INFORMATION
Advising the patient to read the FDA-approved patient labeling (Patient Information)

Neutropenia
Advise patients of the risk of neutropenia. Instruct patients to immediately contact their healthcare provider if they experience fever, chills, or other signs of infection [see Warnings and Precautions (5.1)].

Diarrhea
Advise patients of the risk of diarrhea. Instruct patients to immediately contact their healthcare provider if they experience diarrhea for the first time during treatment; black or bloody stools; symptoms of dehydration such as lightheadedness, dizziness, or faintness; inability to take fluids by mouth due to nausea or vomiting; or inability to get diarrhea under control within 24 hours [see Warnings and Precautions (5.2)].

Hypersensitivity and Infusion-Related Reactions
Inform patients of the risk of serious infusion reactions and anaphylaxis. Instruct patients to immediately contact their healthcare provider if they experience facial, lip, tongue, or throat swelling, urticaria, difficulty breathing, lightheadedness, dizziness, or faintness; inability to take fluids by mouth due to nausea or vomiting; or fever that occur during or within 24 hours following the infusion [see Warnings and Precautions (5.3)].

Nausea/Vomiting
Advise patients of the risk of nausea and vomiting. Premedication according to established guidelines with a two or three drug regimen for prevention of chemotherapy-induced nausea and vomiting (CINV) is also recommended. Additional antiemetics, sedatives, and other supportive measures may also be employed as clinically indicated. All patients should receive take-home medications for preventing and treating delayed nausea and vomiting, with clear instructions. Instruct patients to immediately contact their healthcare provider if they experience uncontrolled nausea or vomiting [see Warnings and Precautions (5.4)].

Embryo-Fetal Toxicity
Advise female patients to contact their healthcare provider if they are pregnant or become pregnant. Inform female patients of the risk to a fetus and potential loss of the pregnancy [see Use in Specific Populations (8.1)].

Contraception
Advise female patients of reproductive potential to use effective contraception during treatment and for 6 months after the last dose of TRODELVY [see Use in Specific Populations (8.3)].

Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of TRODELVY [see Use in Specific Populations (8.3)].

Lactation
Advise women not to breastfeed during treatment and for 1 month after the last dose of TRODELVY [see Use in Specific Populations (8.2)].

Infertility
Advise females of reproductive potential that TRODELVY may impair fertility [see Use in Specific Populations (8.3)].

Manufactured by:
Immunomedics, Inc.
300 The American Road
Morris Plains, NJ 07950, USA
U.S. License No. 1737
**Patient Information**

**TRODELVY®** (troh-DELL-vee)  
(sacituzumab govitecan-hziy)  
for injection, for intravenous use

### What is the most important information I should know about TRODELVY?

**TRODELVY can cause serious side effects, including:**

- **Low white blood cell count (neutropenia).** Low white blood cell counts are common with TRODELVY and can sometimes be severe and cause life-threatening infections that may lead to death. Your healthcare provider should check your blood cell counts during treatment with TRODELVY. If your white blood cell count is too low, your healthcare provider may need to lower your dose of TRODELVY, give you a medicine to help prevent low blood cell count with future doses of TRODELVY, or in some cases may stop TRODELVY. Your healthcare provider may need to give you antibiotic medicines if you develop fever while your white blood cell count is low. **Call your healthcare provider right away if you develop any of the following signs of infection during treatment with TRODELVY:**
  - fever
  - chills
  - shortness of breath
  - burning or pain when you urinate

- **Severe diarrhea.** Diarrhea is common with TRODELVY and can also be severe. Your healthcare provider should monitor you for diarrhea and give you medicine as needed to help control your diarrhea. If you lose too much body fluids (dehydration) your healthcare provider may need to give you fluids and electrolytes to replace body salts. If diarrhea happens later in your treatment, your healthcare provider may check you to see if the diarrhea may be caused by an infection. Your healthcare provider may decrease your dose or stop TRODELVY if your diarrhea is severe and cannot be controlled with anti-diarrheal medicines. **Call your healthcare provider right away:**
  - the first time that you get diarrhea during treatment with TRODELVY
  - if you have black or bloody stools
  - if you have symptoms of losing too much body fluid (dehydration) and body salts, such as lightheadedness, dizziness or faintness
  - if you are unable to take fluids by mouth due to nausea or vomiting
  - if you are not able to get your diarrhea under control within 24 hours

### What is TRODELVY?

TRODELVY is a prescription medicine used to treat adults with breast cancer that is:

- estrogen and progesterone hormone receptor (HR) negative, and human epidermal growth factor receptor 2 (HER2)-negative (also called triple-negative breast cancer), **and**
- that has spread to other parts of the body or cannot be removed by surgery, **and**
- who have received two or more prior treatments, including at least one treatment for metastatic disease. **It is not known if TRODELVY is safe and effective in people with moderate or severe liver problems.** **It is not known if TRODELVY is safe and effective in children.**

**Do not receive TRODELVY if you have had a severe allergic reaction to TRODELVY.** Ask your healthcare provider if you are not sure.

**Before receiving TRODELVY, tell your healthcare provider about all of your medical conditions, including if you:**

- have been told that you carry a gene for uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28. People who carry this gene have an increased risk of getting side effects with TRODELVY, especially low white blood cell counts, a fever while your white blood cell count is low, and low red blood cell counts. **See “What is the most important information I should know about TRODELVY?”**
- have liver problems.
- are pregnant or plan to become pregnant. TRODELVY can harm your unborn baby. Your healthcare provider should check to see if you are pregnant before you start receiving TRODELVY.  
  - Females who can become pregnant should use effective birth control during treatment and for 6 months after your last dose of TRODELVY. Talk to your healthcare provider about birth control choices that may be right for you during this time.
  - Males with a female partner who can become pregnant should use effective birth control during treatment and for 3 months after your last dose of TRODELVY.
Tell your healthcare provider right away if you or your partner become pregnant during treatment with TRODELVY.

- are breastfeeding or plan to breastfeed. It is not known if TRODELVY passes into your breastmilk and can harm your baby. Do not breastfeed during treatment and for 1 month after your last dose of TRODELVY.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Certain medicines may affect the way TRODELVY works.

**How will I receive TRODELVY?**

- Your healthcare provider will give you TRODELVY into your vein through an intravenous (IV) line.
- TRODELVY is given 1 time each week, on Day 1 and on Day 8 of a 21-day treatment cycle.
- You will receive the first dose of TRODELVY over 3 hours. If you tolerate the first dose well, future doses may be given over 1 to 2 hours.
- Before each dose of TRODELVY, you will receive medicines to help prevent infusion reactions, and nausea and vomiting.
- You will be monitored for side effects during and for at least 30 minutes after you receive each infusion of TRODELVY.
- Your healthcare provider may slow down or temporarily stop your infusion of TRODELVY if you have an infusion-related reaction, or permanently stop TRODELVY if you have a life-threatening infusion-related reaction.
- Your healthcare provider will decide how long you will continue to receive TRODELVY.

**What are the possible side effects of TRODELVY?**

TRODELVY can cause serious side effects, including:

- **See “What is the most important information I should know about TRODELVY?”**
- **Allergic and infusion-related reactions.** TRODELVY can cause severe and life-threatening allergic reactions, including during infusion (infusion-related reactions). Tell your healthcare provider or nurse right away if you get any of the following symptoms of an allergic or infusion-related reaction during your infusion of TRODELVY or within 24 hours after you receive a dose of TRODELVY:
  - swelling of your face, lips, tongue, or throat
  - hives
  - skin rash or flushing of your skin
  - difficulty breathing or wheezing
  - lightheadedness, dizziness, feeling faint or pass out
  - chills or shaking chills (rigors)
  - fever

- **Nausea and vomiting.** Nausea and vomiting are common with TRODELVY and can sometimes be severe. Before each dose of TRODELVY, you will receive medicines to help prevent nausea and vomiting. You should be given medicines to take home with you, along with instructions about how to take them to help prevent and treat any nausea and vomiting after you receive TRODELVY. Call your healthcare provider right away if you have nausea or vomiting that is not controlled with the medicines prescribed for you. Your healthcare provider may decide to decrease your dose or stop TRODELVY if your nausea and vomiting is severe and cannot be controlled with anti-nausea medicines.

The most common side effects of TRODELVY include:

- feeling tired or weak
- hair loss
- decreased red blood cell count
- constipation
- rash. See “Allergic and infusion-related reactions” above.
- decreased appetite
- stomach-area (abdominal) pain

TRODELVY may cause fertility problems in females, which could affect your ability to have a baby. Talk to your healthcare provider if fertility is a concern for you.

These are not all of the possible side effects of TRODELVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**General information about the safe and effective use of TRODELVY.**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about TRODELVY that is written for health professionals.

**What are the ingredients in TRODELVY?**

*Active ingredient*: sacituzumab govetecan-hziy

*Inactive ingredients*: 2-(N-morpholino) ethane sulfonic acid (MES), polysorbate 80 and trehalose dihydrate