PRELIMINARY SAFETY, EFFICACY, AND PK/PD CHARACTERIZATION FROM GARNET, A PHASE 1 CLINICAL TRIAL OF THE ANTI–PD-1 MONOCLONAL ANTIBODY, TSR-042, IN PATIENTS WITH RECURRENT OR ADVANCED MSI-H ENDOMETRIAL CANCER

Ana Oaknin,1 Susan L. Ellard2, Charles Leath, III3, Victor Moreno4, Rebecca Kristeleit5, Wei Guo6, Sharon Lu6, David Jenkins6, Kristen McEachern6, Kai Yu Jen6, Steven Dunlap6, Ellie Im6, and Lucy Gilbert7

1Vall d’Hebrón Institute of Oncology (VHIO), Barcelona, Spain; 2British Columbia Cancer Agency and University of British Columbia, Vancouver, BC, Canada; 3University of Alabama at Birmingham, Birmingham, AL; 4START MADRID-FJD, Hospital Fundación Jiménez Díaz, Medical Oncology Department, Madrid, Spain; 5University College London, UCL Cancer Institute, Department of Oncology, London, United Kingdom; 6TESARO, Inc., Waltham, MA; 7McGill University Health Centre, Montreal, QC, Canada
**BACKGROUND**

- TSR-042 is an investigational, humanized anti-programmed death (PD)-1 monoclonal antibody that binds with high affinity to the PD-1 receptor and effectively blocks its interaction with the PD-1 ligands PD-L1 and PD-L2.

- TSR-042 has a safety profile characteristic of approved PD-1 inhibitors and is the only anti-PD-1 therapy administered as a monotherapy every 3 weeks (Q3W) for 4 doses then Q6W until disease progression.

- The ongoing GARNET trial is evaluating TSR-042 as monotherapy in patients with advanced solid tumors, including endometrial cancer (MSI-H and MSS) and non-small cell lung cancer.

**GARNET Trial**

**Part 2B Key Objectives**
- Evaluate safety and tolerability at the RP2D in advanced solid tumors
- Objective response rate (ORR), duration of response (DOR), and DOR per irRECIST assessed by investigators
- To further characterize the pharmacokinetic profile and receptor occupancy (RO) of TSR-042
- **Primary Efficacy Endpoints**
  - ORR and DOR per irRECIST assessed by investigators

**Parts 1 and 2A Completed**

- **Part 1: DLT-Based Dose Escalation**
  - 1-10 mg/kg Q2W
  - N=21, all comers

- **Part 2A: Fixed-Dose Safety Cohorts**
  - 500 mg Q3W or 1000 mg Q6W
  - N=13, all comers

**Part 2B: Expansion Cohorts at RP2D Ongoing**

- **MSI-H Endometrial Cancer**
  - N=65

- **Endometrial Cancer (MSS)**
  - N=65

- **NSCLC**
  - N=65

- **Nonendometrial MSI-H Basket**
  - N=100

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NCT02715284
DLT=dose-limiting toxicity; MSI-H=microsatellite instability-high; EC=endothelial cancer; MSS=microsatellite stable; NSCLC=non-small cell lung cancer; PK=pharmacokinetic; Q2W=every 2 weeks; Q6W=every 6 weeks; RP2D=recommended phase 2 dose.

RESULTS

SAFETY<sup>a</sup>

- Thirty-five patients with MSI-H EC received at least one treatment with TSR-042
- The safety profile of the MSI-H EC cohort was consistent with the safety profile seen in the overall GARNET study
- Treatment-related TEAEs were reported in 65.7% of patients, grade ≥3 treatment-related AEs were reported in 11.4%
- irAEs related to anti-PD-1 therapies<sup>1</sup> were infrequent

EFFICACY

- Twenty-five patients with MSI-H EC were evaluable
- The overall response rate (including both confirmed and unconfirmed responses) was 52% (95% CI: 31.3, 72.2)
- Ten of the 13 responses (77%) are ongoing. One partial response has continued for >60 weeks
- 11 responders (85%) are still receiving treatment
- Two patients had DOR >6 months
- At RP2D, TSR-042 maintained at least a 7.8-fold margin for full RO through the course of treatment

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**Grade ≥3 Treatment-Related TEAEs, Preferred Term**

<table>
<thead>
<tr>
<th>Subjects with at least 1 treatment-related grade ≥3 TEAE, n (%)</th>
<th>MSI-H EC (n=35)</th>
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<tbody>
<tr>
<td>Alanine aminotransferase increased</td>
<td>1 (2.9)</td>
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<tr>
<td>Anemia</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>1 (2.9)</td>
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<tr>
<td>Neutropenia</td>
<td>1 (2.9)</td>
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**Best Overall Response by irRECIST**

<table>
<thead>
<tr>
<th>Complete response&lt;sup&gt;a&lt;/sup&gt;, n (%)</th>
<th>MSI-H EC (n=25)</th>
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<tbody>
<tr>
<td>1 (4)</td>
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<table>
<thead>
<tr>
<th>Partial response&lt;sup&gt;a&lt;/sup&gt;, n (%)</th>
<th>MSI-H EC (n=25)</th>
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<tbody>
<tr>
<td>12 (48)</td>
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<tr>
<th>Stable disease, n (%)</th>
<th>MSI-H EC (n=25)</th>
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<tr>
<td>2 (8)</td>
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<tr>
<th>Progressive disease, n (%)</th>
<th>MSI-H EC (n=25)</th>
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<tr>
<td>7 (28)</td>
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<tr>
<th>Not evaluated, n (%)</th>
<th>MSI-H EC (n=25)</th>
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<tbody>
<tr>
<td>3 (12)</td>
<td></td>
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<thead>
<tr>
<th>Overall response rate&lt;sup&gt;a&lt;/sup&gt;, % (95% CI)</th>
<th>MSI-H EC (n=25)</th>
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<tr>
<td>52 (31.3, 72.2)</td>
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<tr>
<th>Disease control rate&lt;sup&gt;a,b&lt;/sup&gt;, % (95% CI)</th>
<th>MSI-H EC (n=25)</th>
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<tr>
<td>60 (38.7, 78.9)</td>
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<sup>a</sup>Serious treatment-related TEAEs were reported in 2 patients (5.7%).

<sup>b</sup>irCR+irPR+uirPR+irSD.

<sup>a</sup>Responses include both confirmed and unconfirmed responses.

CR=complete response; PR=partial response; SD=stable disease.

Preliminary efficacy data indicates robust activity of TSR-042 in MSI-H EC patients with advanced disease who were previously treated with platinum-based therapy.

Preliminary safety findings indicate that TSR-042 is safe and well tolerated, with a profile characteristic of approved PD-1 inhibitors.

Safety and efficacy data for TSR-042 at the RP2D support the unique and convenient dosing schedule of 500 mg Q3W for the first 4 cycles and 1000 mg Q6W thereafter.

Maximal RO was achieved at the RP2D and maintained through the course of treatment.

**TUMOR RESPONSE**

**CONCLUSIONS**

Depth of Response

- Preliminary efficacy data indicates robust activity of TSR-042 in MSI-H EC patients with advanced disease who were previously treated with platinum-based therapy.
- Preliminary safety findings indicate that TSR-042 is safe and well tolerated, with a profile characteristic of approved PD-1 inhibitors.
- Safety and efficacy data for TSR-042 at the RP2D support the unique and convenient dosing schedule of 500 mg Q3W for the first 4 cycles and 1000 mg Q6W thereafter.
- Maximal RO was achieved at the RP2D and maintained through the course of treatment.