Background

- **Adaptive cell transfer (ACT)** using autologous tumor-infiltrating lymphocytes (TILs) has been shown to be effective for the treatment of advanced metastatic melanoma, and other solid tumors with high tumor mutational burden.1,2

- **Iovance TIL cell therapy (LN-144 Gen 3)** and LN-145, has demonstrated efficacy and safety in clinical trials for several high unmet medical need patient populations, specifically unresectable or persistent cervical cancer, and in head and neck squamous cell carcinoma (PHNDCX)3,4.

- **Further**, TIL cell therapy has shown evidence of efficacy in metastatic non-small cell lung cancer (NSCLC) in a Phase 1 study in combination with nivolumab.5,6,7

Iovance TIL Manufacturing

- **The one-time Iovance TIL cell therapy requires procurement of a small 1.5 cm sample of tumor tissue, which is shipped to a central manufacturing facility where outside of the suppressive tumor microenvironment the TILs are reinvigorated and expanded to approximately 10^7 CD8+ cells. (LN-144, LN-145, LN-145-S1). Manufacturing is a 16 day (Gen 3, Cohort 1C) or 32 day (Gen 2 or LN-145-S1) process.**

Study Overview & Endpoints

- **Approximately 50 clinical sites in the US, Canada, and Europe.**

- **Primary endpoint:** Efficacy and safety, Objective response rate (ORR) per RECIST 1.1 as assessed by investigators.

- **Secondary endpoints:**
  - Additional efficacy parameters.
  - Exploratory endpoints:
    - Predictive and pharmacodynamic biomarkers of clinical response to TIL products.

Study Cohorts

**Figure 2. Study Design**

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Study</th>
<th>Patients</th>
<th>Tumors</th>
<th>TIL, tumor infiltrating lymphocytes</th>
<th>VFC, forced vital capacity</th>
<th>Death</th>
<th>≥1 L</th>
<th>LN144 Gen 3</th>
<th>≥1 L</th>
<th>LN144-S1</th>
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</thead>
<tbody>
<tr>
<td>Cohort 1A: Melanoma</td>
<td>LN-144/145/145-S1</td>
<td>22-day</td>
<td>12</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Cohort 1B: Melanoma</td>
<td>LN-144/145/145-S1</td>
<td>16-day</td>
<td>27</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohort 1C: Melanoma</td>
<td>LN-144/145/145-S1</td>
<td>22-day</td>
<td>37</td>
<td>no</td>
<td>yes</td>
<td>no</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Cohort 2A: Head and Neck</td>
<td>LN-144/145/145-S1</td>
<td>22-day</td>
<td>12</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cohort 2C: NSCLC</td>
<td>LN-144/145/145-S1</td>
<td>22-day</td>
<td>12</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cohort 3C: NSCLC</td>
<td>LN-145/145-S1</td>
<td>16-day</td>
<td>27</td>
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<td>yes</td>
<td>no</td>
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</table>

**IVO-COM-202**

- **IVO-COM-202 (NCT03645928)** is a prospective, open-label, multi-cohort, non-randomized, multicenter Phase 2 study evaluating Iovance TIL therapy (LN-144, LN-145, LN-145-S1) in combination with immune checkpoint inhibitors (ICIs) as a single therapy.

**IOV-COM-202 TIL Regimen**

**Key Inclusion & Exclusion Criteria**

**Inclusion Criteria – All Patients**

- At least 1 resectable lesion.

- Must have remaining measurable disease as defined by RECIST 1.1 following tumor resection.

- ≥15 years of age at the time of consent. Enrollment of patients >70 years of age may be allowed after consultation with the Medical Monitor.

- **ECOG performance status of 0 or 1, and an estimated life expectancy of 6 months.**

**Prior Therapy Criteria**

**Cohort** | **Indication** | **Prior lines of systemic therapy** | **Prior CPI** | **Prior targeted therapy** | **Abbreviations** |
<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>Melanoma (Stage IIC or IV)</td>
<td>≥1</td>
<td>no</td>
<td>yes</td>
<td>IP, ICI, MMKi</td>
</tr>
<tr>
<td>1B</td>
<td>Melanoma (Stage IIC or IV)</td>
<td>0</td>
<td>1</td>
<td>yes</td>
<td>IP, ICI, MMKi</td>
</tr>
<tr>
<td>1C</td>
<td>Melanoma (Stage IIC or IV)</td>
<td>0</td>
<td>≥2</td>
<td>yes</td>
<td>IP, ICI, MMKi</td>
</tr>
<tr>
<td>2A</td>
<td>NSCLC (distant recurrence, or metastasis)</td>
<td>≥2</td>
<td>no</td>
<td>yes</td>
<td>IP, ICI, MMKi</td>
</tr>
<tr>
<td>3A</td>
<td>NSCLC (Stage IV or II)</td>
<td>≥1</td>
<td>no</td>
<td>yes</td>
<td>IP, ICI, MMKi</td>
</tr>
<tr>
<td>3B</td>
<td>NSCLC (Stage II or IV)</td>
<td>≥3</td>
<td>no</td>
<td>yes</td>
<td>IP, ICI, MMKi</td>
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<tr>
<td>3C</td>
<td>NSCLC (Stage II or IV)</td>
<td>0</td>
<td>1/2/3</td>
<td>yes</td>
<td>IP, ICI, MMKi</td>
</tr>
</tbody>
</table>

- *May have received 1 blocking antibody.
- If 1 or 3 lines of 1 blocking antibody were received, 2 are acceptable.
- If ≥2 TKIs were received, 1 blocking antibody is allowed.
- If 1 blocking antibody were received, 1 or 2 TKIs are acceptable.
- May have received BRAF/MAPK or MEKi inhibition positive.

- *May have received BRAF/MEKi or MEKi inhibition positive.
- If BRAF/MEKi received, BRAF/MEKi inhibitors only.
- MEKi inhibition positive.
- *May have received BRAF/MEKi or MEKi inhibition positive.
- If MEKi inhibitors received, MEKi inhibitors only.

**Exclusion Criteria – All Patients**

- Received an organ allograft or prior cell transfer therapy that included a nonmyeloablative or myeloablative chemotherapy regimen within the past 20 years.

- Symptomatic or untreated brain metastases.

- Receiving systemic steroid therapy ≥10 mg/day of prednisone or another steroid equivalent.

- Receiving steroids as replacement therapy for adrenocortical insufficiency ≤10 mg/day of prednisone or another steroid equivalent may be eligible.

- Active medical illnesses(s), which in the opinion of the Investigator, would pose increased risks for study participation.

- Any form of primary immunodeficiency.

- History of hypersensitivity to any component of the study drugs.

- Left ventricular ejection fraction (LVEF) ≤50% or New York Heart Association Class II or higher.

- Patients with respiratory dysfunction or history of smoking require pulmonary function testing and are excluded if not meeting either of foronded expiration volume in 1 second (FEV1) forced vital capacity (FVC) ≥0.7 or FEV1/FVC ≥50%.

- **Cohort-specific Exclusion Criteria**

  - **Cohort 1A, 2A, 3A, and 3C patients may not have a medical history of autoimmune disorders requiring treatment or active management.**

Disclosures

- This study is an extension of a study conducted by Iovance Biotherapeutics, Inc. 
- All other study investigators and sites.

For more information, please contact

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