Iovance IP Leadership Within T-cell Based Immunotherapy

IOVANCE BIOTHERAPEUTICS

Iovance IP Portfolio Summary:

- >400 granted or allowed US and international patents
- >1,000 patents and applications worldwide, including major pharmaceutical markets
- Lifileucel patent rights expected to provide exclusivity into 2042
  - Compositions of matter for TIL products
  - Methods of treatment in a broad range of cancers
  - Manufacturing processes

We established our leadership within T cell-based immunotherapy by building and augmenting the patent rights for our proprietary tumor infiltrating lymphocyte (TIL) technology platform—developed internally and licensed from third parties.

1 Tumor Sample Procurement



TIL from:
- Tumor
- Small biopsy
- Marrow infiltrating lymphocytes
- Peripheral blood lymphocytes
- Frozen tumor technologies
- Remnant TIL and digest processes

3 NMA-LD



4 TIL Infusion



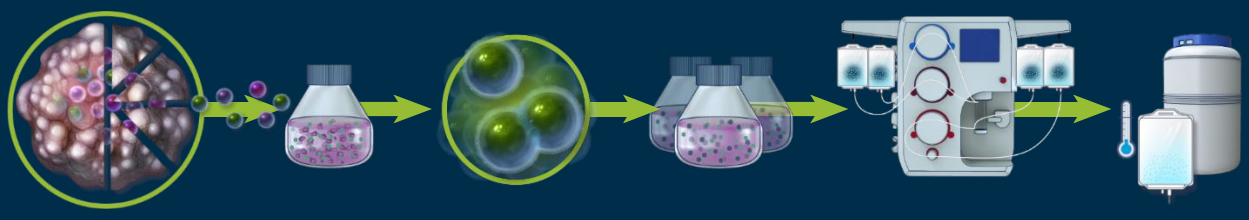
- **Combination of TIL and ICIs including PD-1 antibodies**
- **Patient subpopulations**

5 IL-2 Infusions



IL-2 variants and regimens

2



4

TIL products and compositions: Gen 2, Gen 3, use of co-stimulants, selection of TIL, stable and transient genetic modifications, cryopreservation

Abbreviations: ICI, immune checkpoint inhibitors; IL-2, interleukin 2; IP, intellectual property; NMA-LD, non-myeloablative lymphoid depletion; TIL, tumor infiltrating lymphocytes

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Broad, Iovance-Owned IP Around AMTAGVI® and Other TIL Therapies in Development

Iovance owns more than 100 U.S. patents related to TIL therapy, including patents directed to compositions and methods of treatment in a broad range of cancers, such as U.S. Patent Nos. 10,130,659; 10,166,257; 10,272,113; 10,363,273; 10,398,734; 10,420,799; 10,463,697; 10,517,894; 10,537,595; 10,639,330; 10,646,517; 10,653,723; 10,695,372; 10,894,063; 10,905,718; 10,918,666; 10,925,900; 10,933,094; 10,946,044; 10,946,045; 10,953,046; 10,953,047; 11,007,225; 11,007,226; 11,013,770; 11,026,974; 11,040,070; 11,052,115; 11,052,116; 11,058,728; 11,083,752; 11,123,371; 11,141,434; 11,141,438; 11,168,303; 11,168,304; 11,179,419; 11,202,803; 11,202,804; 11,220,670; 11,241,456; 11,254,913; 11,266,694; 11,273,180; 11,273,181; 11,291,687; 11,293,009; 11,304,979; 11,304,980; 11,311,578; 11,337,998; 11,344,579; 11,344,580; 11,344,581; 11,351,197; 11,351,198; 11,351,199; 11,364,266; 11,369,637; 11,384,337; 11,401,507; 11,433,097; 11,517,592; 11,529,372 ; 11,541,077; 11,631,483; 11,713,446; 11,819,517; 11,857,573; 11,865,140; 11,866,688; 11,939,596; 11,969,444; 11,975,028; 11,981,921; 11,998,568; 12,023,355; 12,024,718; 12,031,157; 12,104,172; 12,121,541; 12,159,700; 12,170,134; 12,188,048; 12,194,061; 12,226,434; 12,226,522; 12,230,378; 12,230,379; 12,233,075; 12,280,140; 12,343,380; 12,453,697; 12,473,532; 12,485,145; 12,495,791; 12,553,029; 12,553,031; 12,558,375; 12,570,959; 12,570,961; 12,611,427; 12,611,428; 12,611,429; 12,617,833; 12,622,927; 12,636,318; 12,642,268; 12,642,816; 12,642,832; 12,648,962; 12,655,389; 12,678,499; and 12,767,928.

Iovance owns U.S. Patent Nos. 12,553,031,12,570,961, and 12,767,928 covering a potency and identity assay for evaluating potency and/or functionality of TIL products, including AMTAGVI®.

Iovance owns U.S. Patent No. 11,819,517 covering methods of using TIL therapy for the treatment of double refractory melanoma in a patient resistant to a PD1 or PD-L1 inhibitor and resistant to a BRAF inhibitor or a BRAF inhibitor and a MEK inhibitor, which methods are free of any TIL process limitations.

Iovance owns U.S. Patent No. 12,553,029 covering methods of using TIL therapy for the treatment of NSCLC in ICI-refractory patients lacking an EGFR driver mutation, which methods are free of any TIL process limitations.

Iovance owns U.S. Patent No. 11,981,921 covering methods of manufacturing TIL product using a rapid expansion process (REP) in the presence of antigen presenting cells (including artificial antigen presenting cells) but without IL-2.

Iovance owns U.S. Patent No. 10,537,595 covering a composition comprising TIL cells and a cryopreservant, free of any TIL process limitations.

Iovance owns U.S. Patent No. 10,653,723 covering a pharmaceutical composition comprising TIL cells and a pharmaceutically acceptable carrier free of any TIL process limitations.

Iovance owns U.S. Patent Nos. 10,905,718 and 10,933,094 covering methods of treating cancer with a pharmaceutical composition comprising TIL cells and a cryopreservant, free of any TIL process limitations.

Iovance owns U.S. Patent Nos. 10,953,046 and 10,953,047 covering methods of treating cancer with a pharmaceutical composition comprising TIL cells and a pharmaceutically acceptable carrier, free of any TIL process limitations.

Iovance owns U.S. Patent Nos. 10,946,044 and 10,946,045 covering methods of treating cancer with TIL therapy, free of any TIL process limitations.

Iovance owns U.S. Patent Nos. 12,226,522 and 12,280,140 covering methods of using TIL therapy and manufacturing TIL products for the treatment of endometrial cancer.

Iovance owns U.S. Patent Nos. 11,384,337, 12,024,718 and 12,495,791 covering methods of manufacturing or using gene-edited TIL product, which methods are free of gene-editing process and target limitations.

Iovance owns U.S. patents covering the use of the combination of TIL therapy and an anti-PD-1 antibody, such as U.S. Patent Nos. 10,272,113 and 12,611,428, or an anti-PD-L1 antibody, such as U.S. Patent No. 11,013,770.

Iovance owns U.S. Patent No. 12,678,499 covering the use of the combination of TIL therapy and pembrolizumab for the treatment of melanoma in anti-PD-1/anti-PD-L1 naïve patients.

Iovance holds an exclusive license to U.S. Patent No. 12,642,832 covering the use of the combination of oncolytic HSV followed by ex vivo expanded T cells for the treatment of melanoma.

Iovance owns EP Patent No. 3710576 and pending U.S. App. No. 18/619,119 covering methods of manufacturing TIL product from FNA or small biopsy, including core biopsy.

Iovance owns PCT Pub. WO/2025/015318, covering TILs expressing membrane-tethered IL-12.

IOVANCE BIOTHERAPEUTICS

Iovance's patent portfolio also includes patents and patent applications relating to:

- TIL cell expansion from core biopsy, small biopsy or fine needle aspirate;
- Frozen tumor-based TIL technologies;
- Remnant TIL and digest TIL compositions and methods;
- Use of co-stimulatory and T cell modulating molecules in TIL therapy and manufacturing;
- Stable and transient genetically-modified TIL therapies;
- Methods of using immune checkpoint inhibitors in combination with TIL therapies;
- TIL cell selection technologies;
- Methods of treating patient subpopulations;
- Cytokine-tethered TIL product, and methods of making and using;
- Artificial antigen presenting cells and use in TIL cell expansion.

Abbreviations: EGFR, epidermal growth factor receptor; ICI, immune checkpoint inhibitor; IL-2, interleukin 2; MEK, Mitogen-activated protein kinase kinase; NSCLC, non-small-cell lung cancer; PD1, programmed cell death protein 1; PD-L1, Programmed death-ligand 1; TIL, tumor infiltrating lymphocytes.

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U.S. Patent/Application Information for Iovance Products:

Therapy	Pursued Indication or use	Composition of Matter	Method of Use		Method of Manufacturing
AMTAGVI®	Patients with metastatic melanoma	US 10,894,063; US 10,398,734; US 10,537,595; US 10,695,372; US 10,653,723; US 11,337,998; US 11,344,579; US 12,194,061; US 12,611,429; US 12,636,318; US 12,655,389	US 10,166,257; US 10,272,113; US 10,463,697; US 10,905,718; US 10,925,900; US 10,933,094; US 10,946,044; US 10,946,045; US 10,953,046; US 10,953,047;	US 11,202,803; US 11,202,804; US 11,241,456; US 11,273,181; US 11,433,097; US 11,517,592; US 11,819,517; US 12,121,541; US 12,622,927; US 12,678,499	US 10,420,799; US 10,639,330; US 10,918,666; US 11,273,180; US 11,291,687; US 11,304,979; US 12,485,145; US 12,553,031; US 12,570,961; US 12,642,816; US 12,767,928
Lifileucel	Patients with NSCLC, sarcoma, HNSCC, cervical cancer or endometrial cancer	US 10,894,063; US 10,398,734; US 10,537,595; US 10,653,723; US 10,695,372; US 11,337,998; US 11,344,579; US 12,194,061; US 12,611,429; US 12,636,318; US 12,655,389; US 11,376,318[b]	US 10,130,659; US 10,166,257; US 10,272,113; US 10,463,697; US 10,363,273; US 10,905,718; US 10,933,094; US 10,946,044; US 10,946,045; US 10,953,046; US 10,953,047; US 11,202,804; US 11,241,456;	US 11,273,181; US 11,433,097; US 12,121,541; US 12,226,522; US 12,553,029; US 12,611,427; US 12,611,428; US 11,077,182[b]; US 11,331,385[b]; US 11,338,032[b]; US 11,376,318[b]	US 10,420,799; US 10,639,330; US 10,918,666; US 11,273,180; US 11,291,687; US 11,304,979; US 12,280,140; US 12,485,145; US 12,553,031; US 12,570,959; US 12,570,961; US 12,642,816; US 12,767,928
IOV-4001 (PD1 KO TIL)	Patients with metastatic melanoma or NSCLC	US 10,537,595; US 10,653,723; US 12,031,157	US 10,905,718; US 10,933,094; US 10,946,044; US 10,946,045; US 10,953,046;	US 10,953,047; US 11,202,804; US 11,819,517; US 12,121,541; US 12,495,791; US 12,642,268	US 11,304,979; US 11,384,337; US 12,024,718; US 12,495,791; US 11,674,155[a]; US 11,891,614[a]
IOV-5001 (Cytokine-Tethered TIL)	Solid tumors, including colorectal cancer, triple-negative breast cancer, and ER^{low} breast cancer	US 12,617,833; US 8,556,882[b]; US 12,157,762[b] WO/2025/015318			US 11,384,337; US 11,981,921; US 12,024,718
IOV-3001 (Next-Generation IL-2)	Supportive therapy for patients treated with TIL	US 12,006,354[c]	US 12,006,354[c]		
IovanceCares™	TIL therapy ordering, chain of custody, supply, and patient support services				US 11,631,483; US 12,159,700; US 12,170,134; US 12,230,378; US 12,230,379

[a]Iovance holds an exclusive license under patents and patent applications of Cellectis covering Iovance's IOV-4001 product.
[b]Iovance holds an exclusive license under patents and patent applications of NIH covering Iovance's IOV-5001 product and a subset of lifileucel-related patents.
[c]Iovance holds an exclusive license under patents and patent applications of Novartis covering Iovance's IOV-3001 product.
Abbreviations: ER, estrogen receptor; HNSCC, head and neck squamous cell carcinoma; IL-2, interleukin 2; KO, knock-out; NSCLC, non-small-cell lung cancer; PD1, programmed cell death protein 1; TIL, tumor infiltrating lymphocytes.
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