Iovance IP Leadership Within T-cell Based Immunotherapy

Iovance IP Portfolio Summary:

- >280 granted or allowed US and international patents
- Compositions of matter for TIL products
- Methods of treatment in a broad range of cancers
- Manufacturing processes
- >1,000 patents and applications worldwide, including major pharmaceutical markets
- Gen 2 patent rights expected to provide exclusivity into 2038
- Additional patent rights expected to provide exclusivity into 2042



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.



Tumor Sample Procurement





NMA-LD





TIL Infusion



- IL-2 Infusions

TIL from:

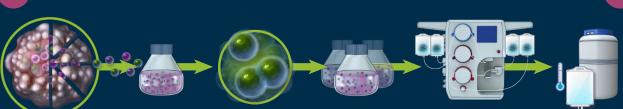
- Tumor
- Small biopsy
- Marrow infiltrating lymphocytes
- Peripheral blood lymphocytes
- Frozen tumor technologies
- Remnant TIL and digest processes

Combination of TIL and ICIs including PD-1 antibodies

Patient subpopulations

IL-2 variants and regimens





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

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

lovance owns more than 90 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; 11,577,592; 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; 12,226,6434; 12,226,522; 12,230,378; 12,230,379; 12,233,075; 12,280,140; and 12,343,380.

lovance also owns U.S. patents covering methods of manufacturing TIL and TIL manufactured from a tumor digest and the use thereof, such as U.S. Patent Nos. 11,007,225; 11,007,226; 11,052,115; 11,052,116; 11,058,728; 11,083,752; 11,123,371; 11,141,438; 11,179,419; 11,202,803; 11,202,804; 11,241,456; 11,254,913; 11,266,694; 11,273,180; 11,273,181; 11,291,687; 11,304,979; 11,304,980; 11,337,998; 11,344,579; 11,529,372; 11,541,077; and others.

Iovance owns U.S. Patent No. 11,819,517 covering methods of using TIL 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.

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

lovance owns U.S. Patent No. 11,384,337 covering methods of manufacturing gene-edited TILs, which methods are free of gene-editing process and target limitations.

lovance owns U.S. Patent No. 11,713,446 covering methods of manufacturing TIL modified to effect transient alteration of expression of one or more proteins.

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

lovance owns a U.S. patent covering methods of treating a cancer patient, wherein one or more tumor specific mutations harbored by the patient has been determined to be a clonal neoantigen.



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

- 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 selection technologies;

US 12,230,379

 Methods of treating patient subpopulations.

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

herapy	Pursued Indication	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 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 10,420,799; US 10,639,330; US 10,918,666; US 11,273,180; US 11,291,687; US 11,304,979
Lifileucel	Patients with NSCLC, 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 11,376,318 (NIH)	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 11,077,182 (NIH); US 11,331,385 (NIH); US 11,338,032 (NIH); US 11,376,318 (NIH)	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
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 11,304,979; US 11,384,337; US 12,024,718; US 11,674,155 (Cellectis); US 11,891,614 (Cellectis)
OV-5001 (Cytokine-Tethered TIL)		US 8,556,882 (NIH)			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 (Novartis)	US 12,006,354 (Novartis)		
IovanceCares™					US 11,631,483; US 12,159,700; US 12,170,134; US 12,230,378;

Abbreviations: HNSCC, head and neck squamous cell carcinoma; KO, knockout; NSCLC, non-small-cell lung cancer; TiL, tumor infiltrating lymphocytes. lovance holds an exclusive license under patents and patent applications of Cellectis covering lovance's IOV-4001 product. lovance holds an exclusive license under patents and patent applications of NIH covering lovance's IOV-5001 product. lovance holds an exclusive license under patents and patent applications of Novartis covering lovance's IOV-3001 product. Amtagivi's and its accompanying design marks, Proleukin®, lovance®, and lovanceCares™ are trademarks and registered trademarks of lovance Biotherapeutics, Inc. or its subsidiaries.

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