Iovance IP Leadership Within T-cell Based Immunotherapy

Iovance IP Portfolio Summary:

- >250 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





IL Infusion



- J
- including PD-1 antibodies

 Patient subpopulations

Combination of TIL and ICIs



IL-2 Infusions

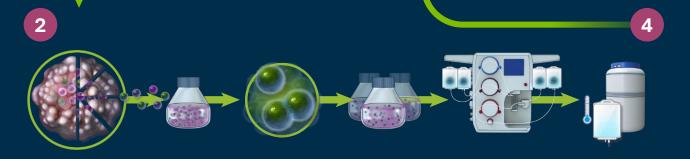


IL-2 variants and regimens

TIL from:

- Tumor
- Small biopsy
- Marrow infiltrating lymphocytes
- Peripheral blood lymphocytes
- Frozen tumor technologies

Remnant TIL and digest processes



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 at least 80 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; 11,141,438; 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; 11,304,979; 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; 11,433,097; 11,517,592; 11,529,372; 11,541,077; 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; 12,023,355; 12,024,718; 12,031,157; 12,104,172; 12,121,541; 12,159,700; 12,170,134; 12,188,048; and 12,194,061.

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. U.S. Patent No. 11,058,728 specifically covers a method of treatment using expanded TILs manufactured from a tumor digest where the expansion steps through the step of cryopreservation of the infusion bag having a harvested TIL population are performed within about 24 days. U.S. Patent No. 11,123,371 specifically covers a cryopreserved TIL composition comprising expanded TILs manufactured from a cryopreserved tumor digest where the expansion steps through the step of cryopreservation of the infusion bag having a harvested TIL population are performed within about 24 days. U.S. Patent No. 11,141,438 specifically covers an expanded population of TILs manufactured from a cryopreserved tumor digest where the expansion steps through the harvest step are performed within about 24 days. U.S. Patent No. 11,179,419 specifically covers a method for expanding TILs from a cryopreserved tumor digest where the expansion steps through the step of cryopreservation of the infusion bag having a harvested TIL population are performed within about 24 days.

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

Iovance 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'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;
- Methods of treating patient subpopulations.

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

Therapy	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 10,993,094; 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 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
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)
IOV-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	WO 2018/215936A1 (Novartis); US 2020/270334A1 (Novartis)	WO 2018/215936A1 (Novartis); US 2020/270334A1 (Novartis)		WO 2018/215936A1 (Novartis); US 2020/270334A1 (Novartis)
IOV-2001 (PBL)	Patients with CLL or SLL	WO 2020/180733 A1; US 2020/0224161 A1; US 2020/0347350 A1	WO 2020/180733 A1; US 2020/0224161 A1; US 2020/0347350 A1		WO 2020/180733 A1; US 2020/0224161 A1; US 2020/0347350 A1
IovanceCares™					US 11,631,483; US 12,159,700; US 12,170,134

Abbreviations: CLL, chronic lymphocytic leukemia; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small-cell lung cancer; PBL, peripheral blood lymphocytes; SLL, small lymphocytic leukemia; TIL, tumor infiltrating lymphocytes.

lovance holds an exclusive license under patents and patent applications of Cellectis covering lovance's IOV-4001 product.

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