IOVANCE BIOTHERAPEUTICS

Comparability study considerations in the development and approval of AMTAGVI™ (lifileucel)

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ADVANCING IMMUNO-ONCOLOGY

Forward-Looking Statements

Certain matters discussed in this presentation are “forward-looking statements” of Iovance Biotherapeutics, Inc. (hereinafter referred to as the “Company,” “we,” “U.S.,” or “our”) within the meaning of the Private Securities Litigation Reform Act of 1995 (the “PSLRA”). Without limiting the foregoing, we may, in some cases, use terms such as “predicts,” “believes,” “potential,” “continue,” “estimates,” “anticipates,” “expects,” “plans,” “intends,” “forecast,” “guidance,” “outlook,” “may,” “could,” “might,” “will,” “should,” or other words that convey uncertainty of future events or outcomes and are intended to identify forward-looking statements. Forward-looking statements are based on assumptions and assessments made in light of management’s experience and perception of historical trends, current conditions, expected future developments, and other factors believed to be appropriate. Forward-looking statements in this press release are made as of the date of this press release, and we undertake no duty to update or revise any such statements, whether as a result of new information, future events or otherwise. Forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties, and other factors, many of which are outside of our control, that may cause actual results, levels of activity, performance, achievements, and developments to be materially different from those expressed in or implied by these forward-looking statements. Important factors that could cause actual results, developments, and business decisions to differ materially from forward-looking statements are described in the sections titled "Risk Factors" in our filings with the U.S. Securities and Exchange Commission, including our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, and include, but are not limited to, the following substantial known and unknown risks and uncertainties inherent in our business: the risks related to our ability to successfully commercialize our products, including Amtagvi and Proleukin, for which we obtain U.S. Food and Drug Administration (“FDA”), European Medicines Agency (“EMA”), or other regulatory authority approval; the risk that the EMA or other regulatory authorities may not approve or may delay approval for our biologics license application (“BLA”) submission for lifileucel in metastatic melanoma; the acceptance by the market of our products, including Amtagvi and Proleukin, and their potential pricing and/or reimbursement by payors, if approved (in the case of our product candidates), in the U.S. and other international markets and whether such acceptance is sufficient to support continued commercialization or development of our products, including Amtagvi and Proleukin, or product candidates, respectively; our ability or inability to manufacture our therapies using third party manufacturers or at our own facility may adversely affect our commercial launch; the results of clinical trials with collaborators using different manufacturing processes may not be reflected in our sponsored trials; the risk regarding the successful integration of the recent Proleukin acquisition; the risk that the successful development or commercialization of our products, including Amtagvi and Proleukin, may not generate sufficient revenue from product sales, and we may not become profitable in the near term, or at all; the risk that future competitive or other market factors may adversely affect the commercial potential for Amtagvi or Proleukin; the risks related to the timing of and our ability to successfully develop, submit, obtain, or maintain FDA, EMA, or other regulatory authority approval of, or other action with respect to, our product candidates; whether clinical trial results from our pivotal studies and cohorts, and meetings with the FDA, EMA, or other regulatory authorities may support registrational studies and subsequent approvals by the FDA, EMA, or other regulatory authorities, including the risk that the planned single arm Phase 2 IOV-LUN-202 trial may not support registration; preliminary and interim clinical results, which may include efficacy and safety results, from ongoing clinical trials or cohorts may not be reflected in the final analyses of our ongoing clinical trials or subgroups within these trials or in other prior trials or cohorts; the risk that enrollment may need to be adjusted for our trials and cohorts within those trials based on FDA and other regulatory agency input; the risk that the changing landscape of care for cervical cancer patients may impact our clinical trials in this indication; the risk that we may be required to conduct additional clinical trials or modify ongoing or future clinical trials based on feedback from the FDA, EMA, or other regulatory authorities; the risk that our interpretation of the results of our clinical trials or communications with the FDA, EMA, or other regulatory authorities may differ from the interpretation of such results or communications by such regulatory authorities (including from our prior meetings with the FDA regarding our non-small cell lung cancer clinical trials); the risk that clinical data from ongoing clinical trials of Amtagvi will not continue or be repeated in ongoing or planned clinical trials or may not support regulatory approval or renewal of authorization; the risk that unanticipated expenses may decrease our estimated cash balances and forecasts and increase our estimated capital requirements; the effects of the COVID-19 pandemic; and other factors, including general economic conditions and regulatory developments, not within our control.

AMTAGVI™
(lifileucel) Suspension for IV infusion

First and only one-time, individualized T cell therapy approved by FDA for a solid tumor cancer

IOVANCE BIOTHERAPEUTICS

Iovance is a Global Leader in Innovating, Developing and Delivering TIL Therapy for Patients with Cancer

Commercial Products

AMTAGVI™ (lifileucel) Suspension for IV infusion

PROLEUKIN® (aldesleukin)

600+
Patients Treated with Iovance TIL

100+
Amtagvi Patients Enrolled by 5/9/24

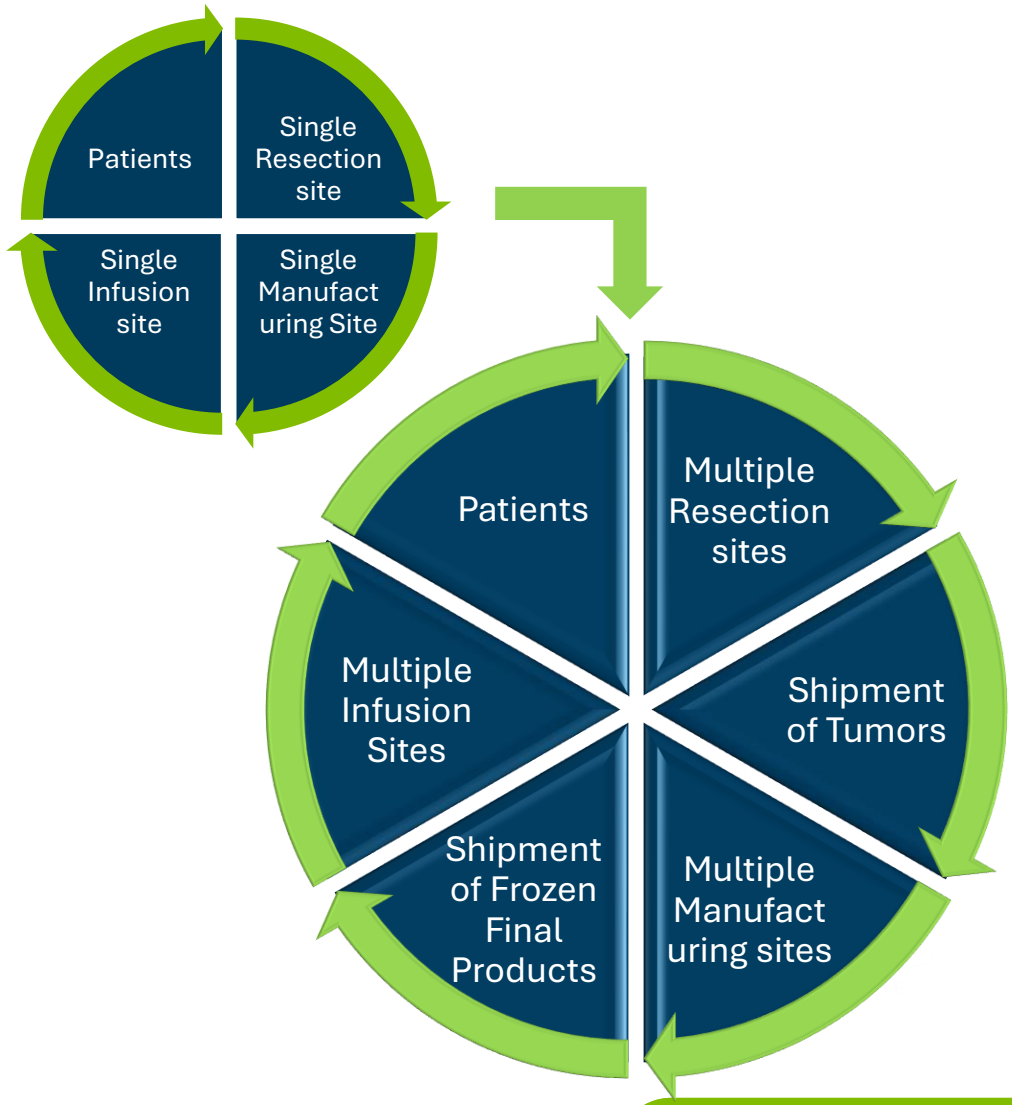
50
Authorized Treatment Centers by 5/28/2024

2 Registrational Clinical Trials

7 Active Clinical Trials

5 Tumor Types in Clinic

3 Fast Track **1** BTD **1** RMAT
Designations

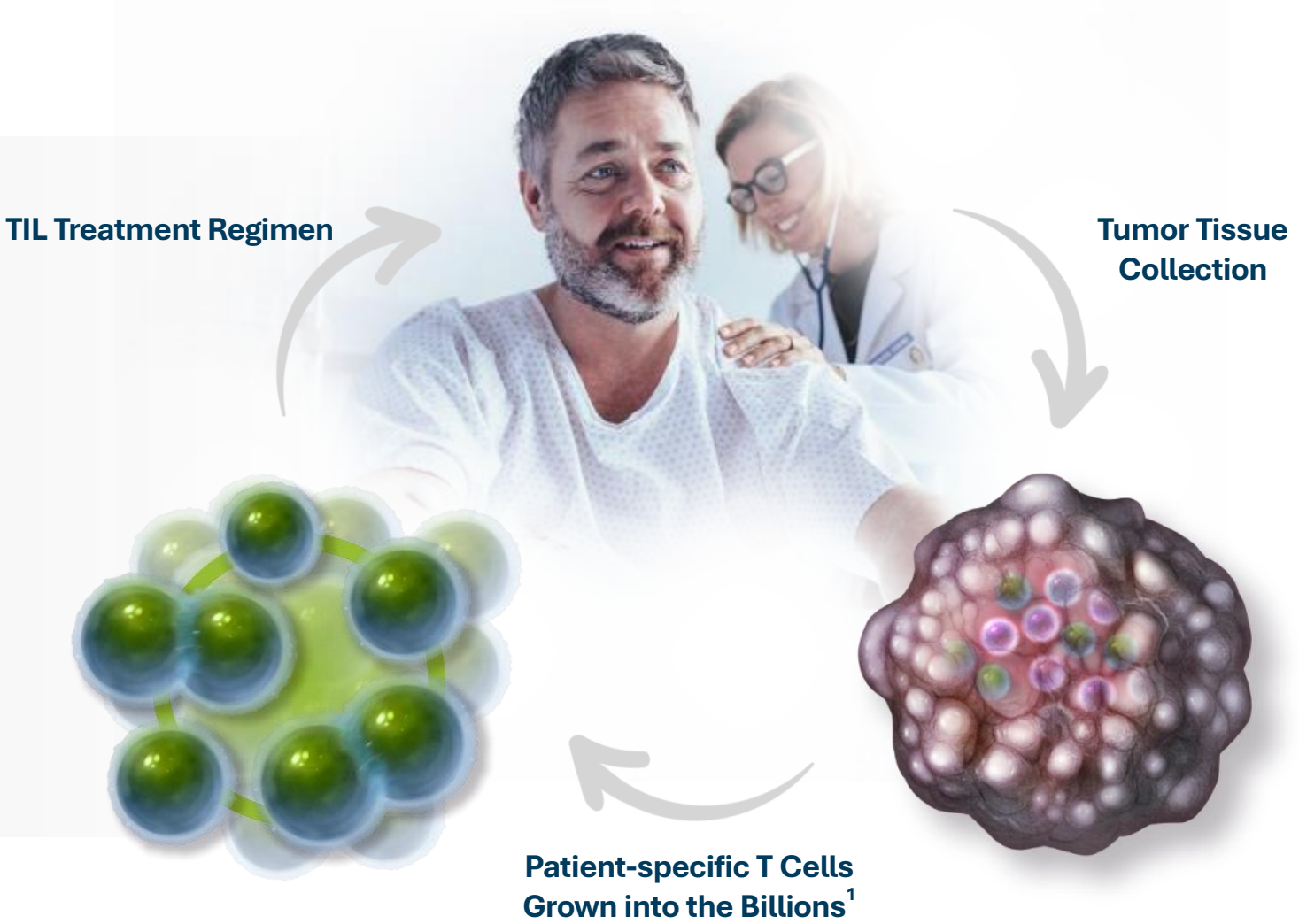


Abbreviations: BTD: Breakthrough Therapy Designation; RMAT: Regenerative Medicine Advanced Therapy Designation

Tumor Infiltrating Lymphocytes (TIL): Leading Cell Therapy Platform for Solid Tumors

TIL – Unique Proposed Mechanism of Action

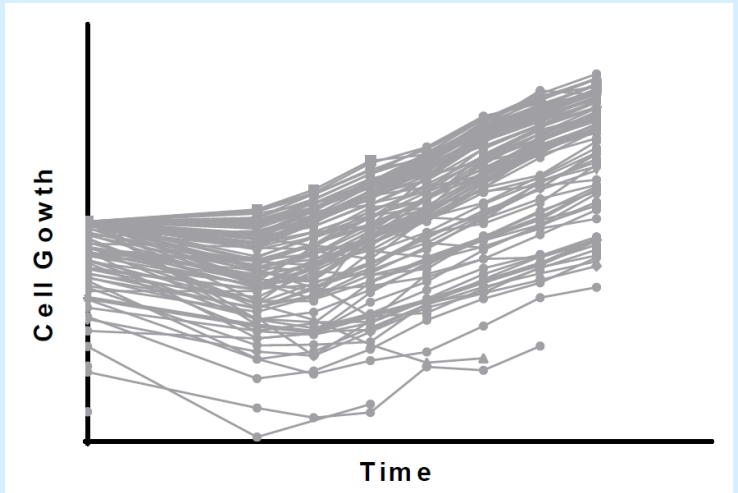
- Individualized
- One-time therapy
- Deploys the patient's own T cells to fight cancer

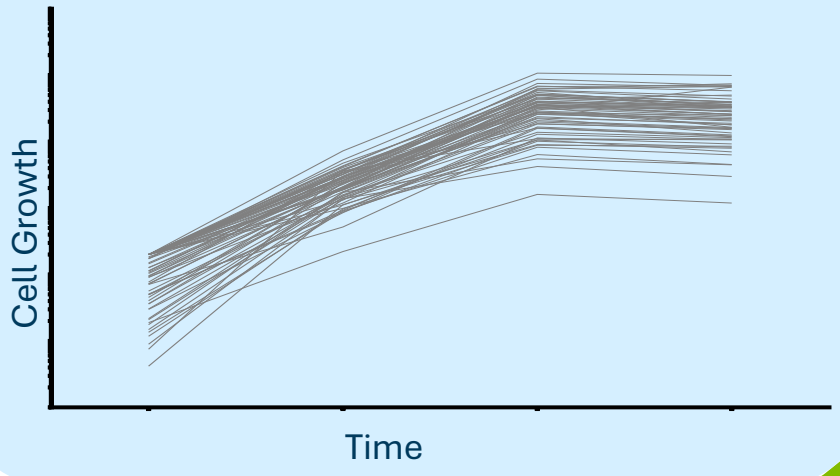


1. Amtagvi USPI

TIL vs CAR-T Similarities

- **T-cell centric processes**
- **1 lot = 1 patient, and patient is waiting for the product**
  - Right First Time, On Time, All the Time
  - Process designed to “Scale out” rather than “Scale up” to meet the demand
  - Chain of Identity and Chain of Custody controls in Supply Chain
- **No terminal sterilization**
  - Sterility assurance has to be built into the process from start to finish
- **Patient to patient variability and cellular heterogeneity**





TIL vs CAR-T Differences

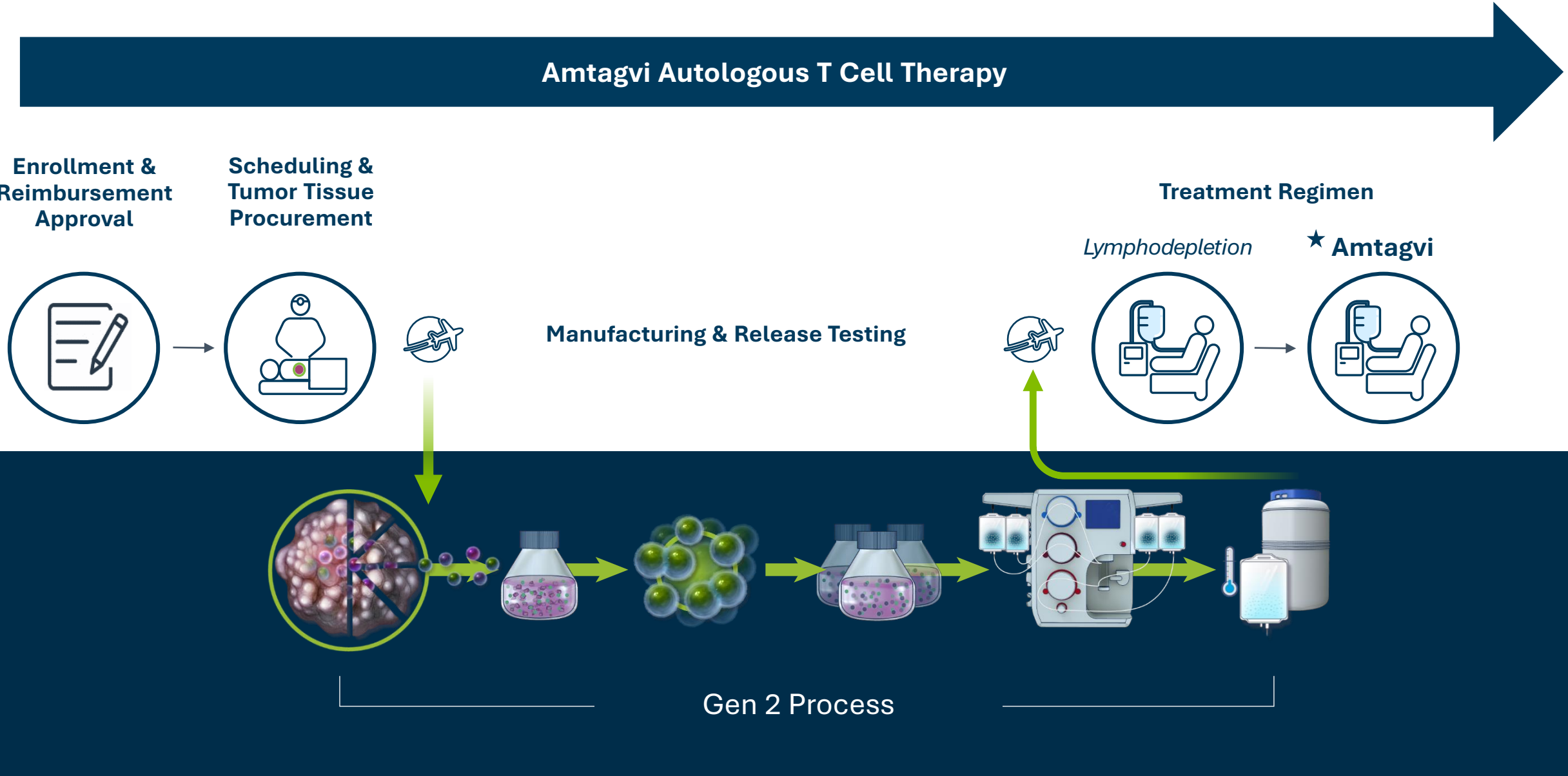
Amtagvi™ is not genetically modified, while CAR-T cells are genetically modified

- TIL are polyclonal, and tumor reactive clones are unique for each patient

Starting material is resected tumor (vs leukapheresis) with unique attributes.

- Choice of optimal anatomic resection site, size of resected lesion
- Ex vivo prosection and preparation of the lesion is crucial to ensure cell expansion success
  - Remove necrotic portions
  - Variability in levels of TIL infiltrate between tumor fragments
- “Fresh” starting material
- No Healthy Donor Surrogate
- Limited Availability of Starting Material
  - Limited number of replicate runs
  - Difficult to estimate process variability independent of patient variability

Iovance TIL Cell Therapy Patient Journey



Iovance Cell Therapy Center: iCTC

Built-to-suit custom facility in Navy Yard Philadelphia

136,000 ft^2, $85M investment

LEED gold certification for core and shell building

Honorable Mention Winner: 2022 ISPE Facility of the Year Awards

Control to optimize capacity, quality & COGS

Clinical supply initiated 3Q21

Commercial manufacturing site 2Q24

Leading Cell Therapy Manufacturing Facility

IOVANCE BIOTHERAPEUTICS
CELL THERAPY CENTER

FOYA 2022
ISPE Facility of the Year Awards
CATEGORY WINNER
Honorable Mention

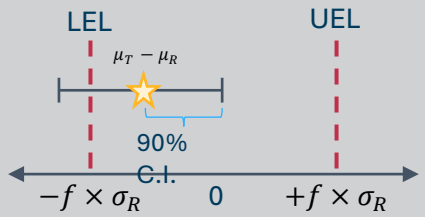
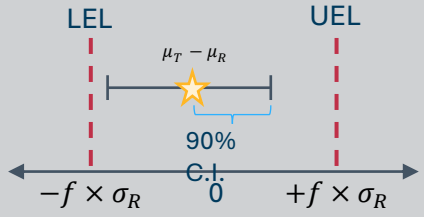
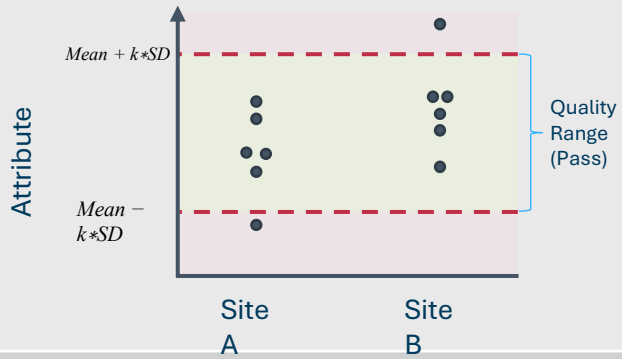
Site to Site Comparability Study

- Study design per ICH Q5E, using a head-to-head design
- Site with the most clinical manufacturing experience was the reference site
- Limitations with starting material overcome by:
  - Establishing comparability in stage-wise manner
  - Implementing a cryopreserved intermediate
  - Demonstrating comparability of cryopreserved intermediate to continuous process
- Large “n” to appropriately power the study, guided by recommendations in Tsong et al (2017)

- Tsong, Y, Dong, X, Shen, M. Development of statistical methods for analytical similarity assessment. Journal of Biopharmaceutical Statistics, 2017, 27(2): 197-205

Statistical Evaluation Methodology

- Test attributes were divided into three tiers based on criticality

Tier	Attribute	Assessment Type	Statistical Method
Tier 1	○ **DP Release attributes**	Two One-Sided T-test (equivalence method)	H_0: sites are different  H_1: sites are **not** different  LEL – Lower Equivalence Limit; UEL – Upper Equivalence Limit; f – multiplication factor; σ_R - Reference population standard deviation
Tier 2	○ **In-process attributes** ○ **Extended characterization**	Quality Range approach	 • Mean and SD are of the reference population • k = 2.58 to account for 99% of population
Tier 3	○ **Post-thaw stability**	Visual/ graphical/ tabular	n/a

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Thank You

Iovance Cell Therapy Center - *i*CTC

The Navy Yard, Philadelphia

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