Alliance for Regenerative Medicine

Advancing cancer care through innovation in cell-based immuno-oncology

Takeaways from a scientific workshop

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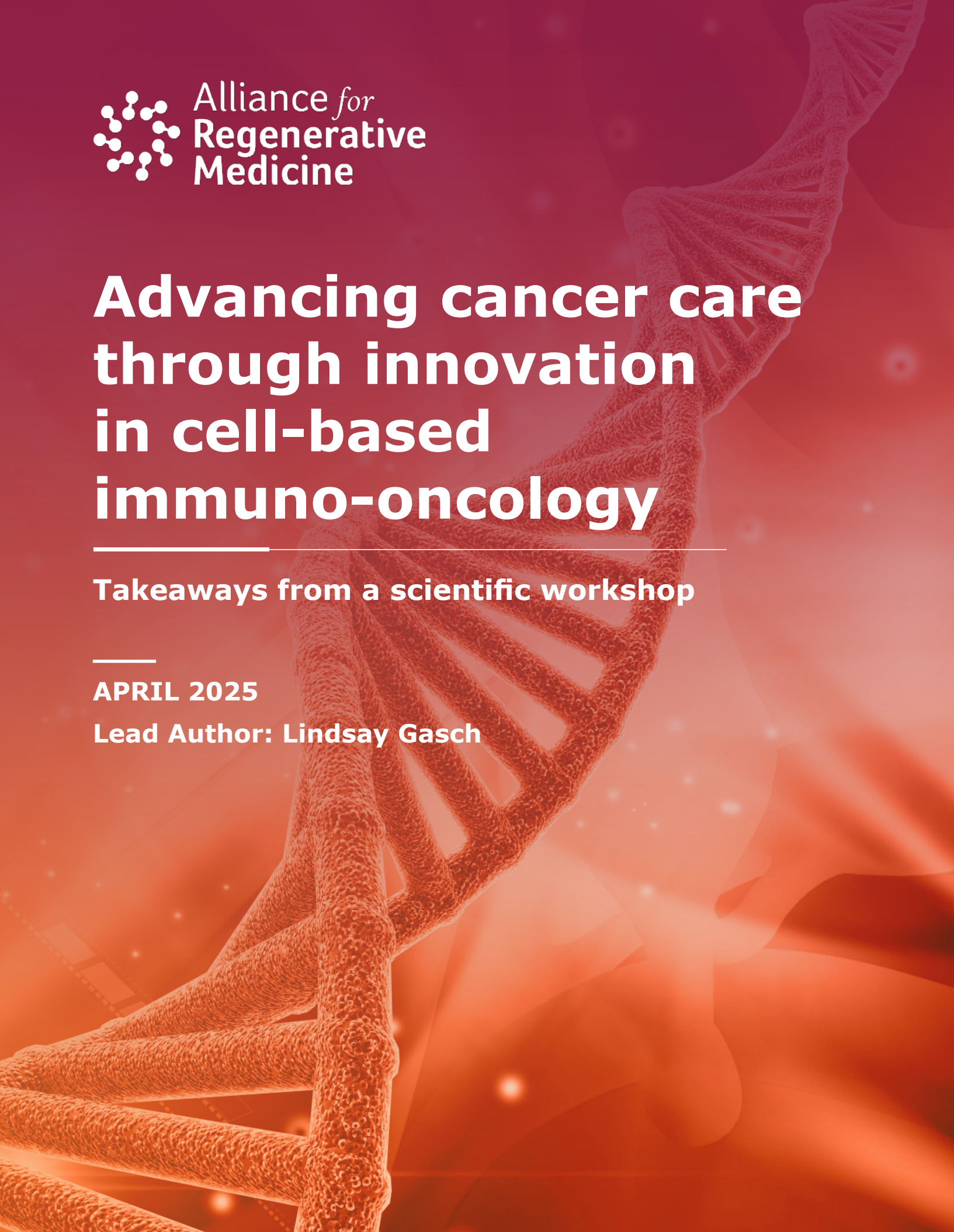


TABLE OF CONTENTS

INTRODUCTION

Adoptive cell therapy, the use of immune cells to help fight disease, is seeing rapid growth in the oncology industry, with indications now spanning hematological and solid malignancies. From September 5th-6th, 2024, the **Alliance for Regenerative Medicine (ARM)** held a 1.5-day workshop on cell-based immuno-oncology (IO) to explore the current and future state of autologous and allogeneic cellular immunotherapies for treating cancer. The workshop brought together academic experts, therapeutic developers, regulatory representatives, and other key stakeholders from across the industry (see the Appendix for a full list of presenters and panelists).

The goals of the workshop were to (1) share clinical program updates, success stories, and key advances in manufacturing; (2) discuss how to resolve barriers to patient access for commercial products; (3) review novel next-generation T cell-based and innate approaches to IO development; and (4) discuss new and upcoming regulatory guidance documents and their applicability to cell-based–IO development. [i] Many topics were discussed in the context of autologous CAR T-cell therapies for hematological malignancies, given their stronger presence in the industry. However, significant attention was also paid to allogeneic approaches, applications in solid tumors, and exploration of novel cell types and targets. Presenters and panelists briefly explored the extension of adoptive cell therapies beyond oncology indications. The importance of patient centricity emerged across topics and is discussed throughout the whitepaper.

For definition of all abbreviations used in this whitepaper, please see the appendix.

[i] Except where noted (e.g., publications cited), the information presented at the workshop and included in this whitepaper has not been subject to peer review.

SUCCESS STORIES AND RECENT PROGRESS

Continued growth of cell-based IO

In line with FDA's 2019 prediction that the Agency will be approving 10 to 20 cell and gene therapy (CGT) products a year by 2025,[1] adoptive cell therapies experienced continued growth in 2023 and 2024. Notable cell-based IO 2024 milestones include the approval of 2 CAR T-cell therapies into earlier lines of therapy for multiple myeloma (CARVYKTI®, 2nd line; ABECMA®, 3rd line) and the first approvals of adoptive cell therapies for solid-tumor indications (AMTAGVI™ for metastatic melanoma; TECELRA® for synovial sarcoma). With commercially approved cell-therapy products for hematology and solid-tumor indications **(Box 1)** the global cell-based IO industry is on track to treat over 10,000 patients this year for the first time.[2]

Box 1. Approved cell-based IO products as of January 2025

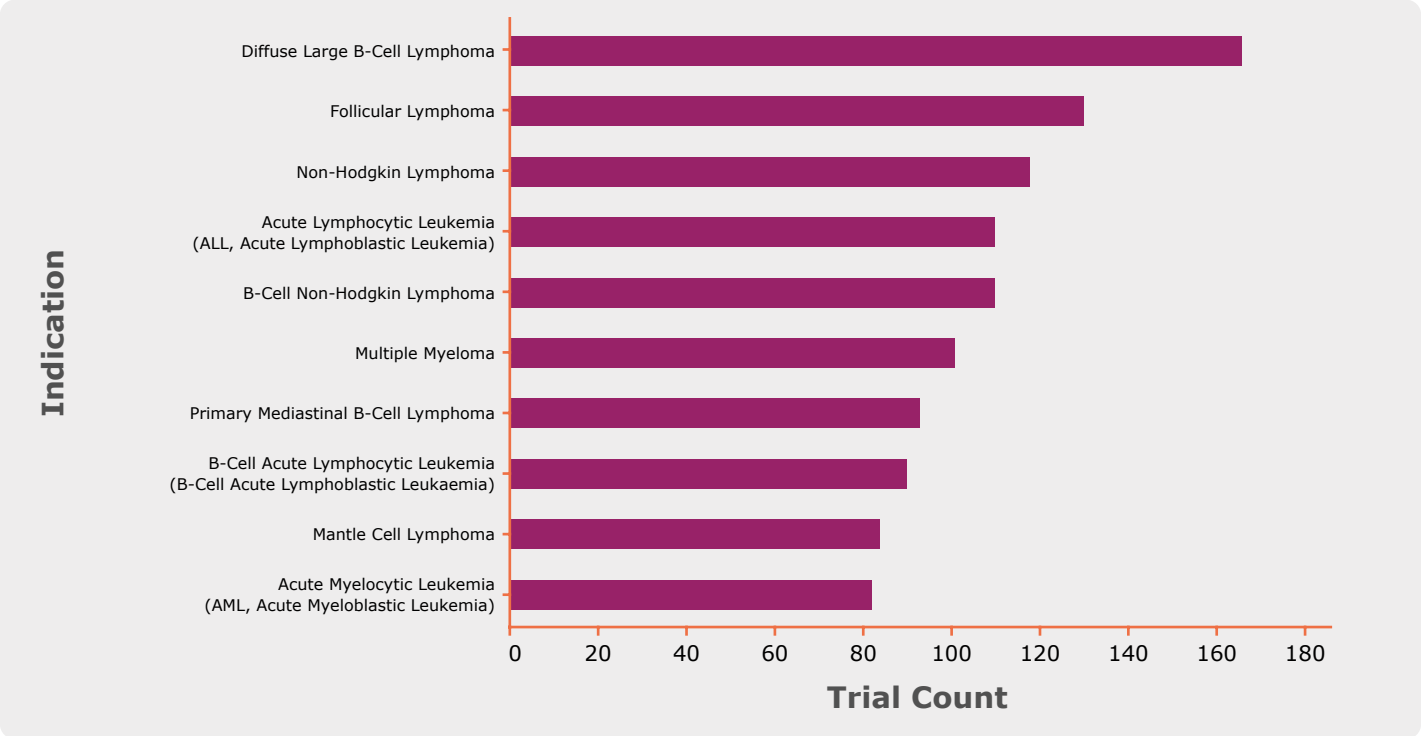
Product	Cell Type	Country of approval	Indication	Year First Approved*
Abecma	BCMA CAR-T	United States Canada Japan European Union Israel Switzerland	R/R multiple myeloma R/R multiple myeloma R/R multiple myeloma R/R multiple myeloma R/R multiple myeloma R/R multiple myeloma	2021 2021 2022 2021 2023 2023
Amtagvi	TIL	United States	Metastatic melanoma	2024
Aucatzyl	CD19 CAR-T	United States	R/R B-ALL	2024
Breyanzi	CD19 CAR-T	United States Japan European Union Canada	R/R LBCL, R/R CLL or SLL, R/R FL, R/R MCL R/R LBCL, R/R FL, R/R MCL R/R DLBCL, R/R PMBCL R/R DLBCL	2021 2021 2022 2022
Carteyva	CD19 CAR-T	China	R/R FL, R/R MCL	2022
Carvykti	BCMA CAR-T	United States European Union Brazil Japan China Canada	R/R multiple myeloma R/R multiple myeloma R/R multiple myeloma R/R multiple myeloma R/R multiple myeloma R/R multiple myeloma	2022 2022 2022 2022 2024 2024
Ebvallo	T-Cell	European Union	R/R EBV+ PTLD	2022

Product	Cell Type	Country of approval	Indication	Year First Approved*
Inaticabtagene Autoleucel	CD19 CAR-T	China	R/R B-ALL	2023
Kymriah	CD19 CAR-T	United States European Union Japan Canada Singapore Australia UK	R/R FL, R/R DLBCL, R/R ALL R/R FL, R/R DLBCL, R/R ALL R/R DLBCL, R/R ALL R/R B-ALL R/R DLBCL, R/R B-ALL R/R DLBCL R/R B-ALL	2017 2018 2019 2018 2021 2018 2018
Tecartus	CD19 CAR-T	United States European Union Brazil	R/R ALL, R/R MCL R/R ALL, R/R MCL R/R ALL, R/R MCL	2020 2019 2022
Tecelra	TCR	United States	Advanced synovial sarcoma	2024
Yescarta	CD19 CAR-T	United States European Union United Kingdom China Canada Japan Brazil Australia Israel Singapore Switzerland	R/R LBCL, R/R DLBCL, R/R PMBCL, R/R HGBCL, R/R FL R/R HGBCL, R/R DLBCL, R/R PMBCL, R/R FL R/R HGBCL, R/R DLBCL, R/R PMBCL, R/R FL R/R LBCL, R/R DLBCL, R/R PMBCL, R/R HGBCL R/R DLBCL or R/R HGBCL R/R LBCL, R/R DLBCL, R/R PMBCL, R/R HGBCL R/R LBCL R/R LBCL R/R LBCL R/R LBCL R/R LBCL	2017 2018 2018 2021 2023 2022 2022 2022 2023 2023 2023

* The list notes when the therapy was first approved, but includes all indications it is currently approved for, some of which were approved at a later date.
R/R, relapsed or refractory; B-ALL, B-cell acute lymphoblastic leukemia; LBCL, large B-cell lymphoma; CLL, chronic lymphocytic leukemia; SLL, small lymphocytic lymphoma; FL, follicular lymphoma; MCL, mantle cell lymphoma; DLBCL, diffuse large B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma; HGBCL, high-grade B-Cell lymphoma; EBV+ PTLD, Epstein-Barr virus positive post-transplant lymphoproliferative disease

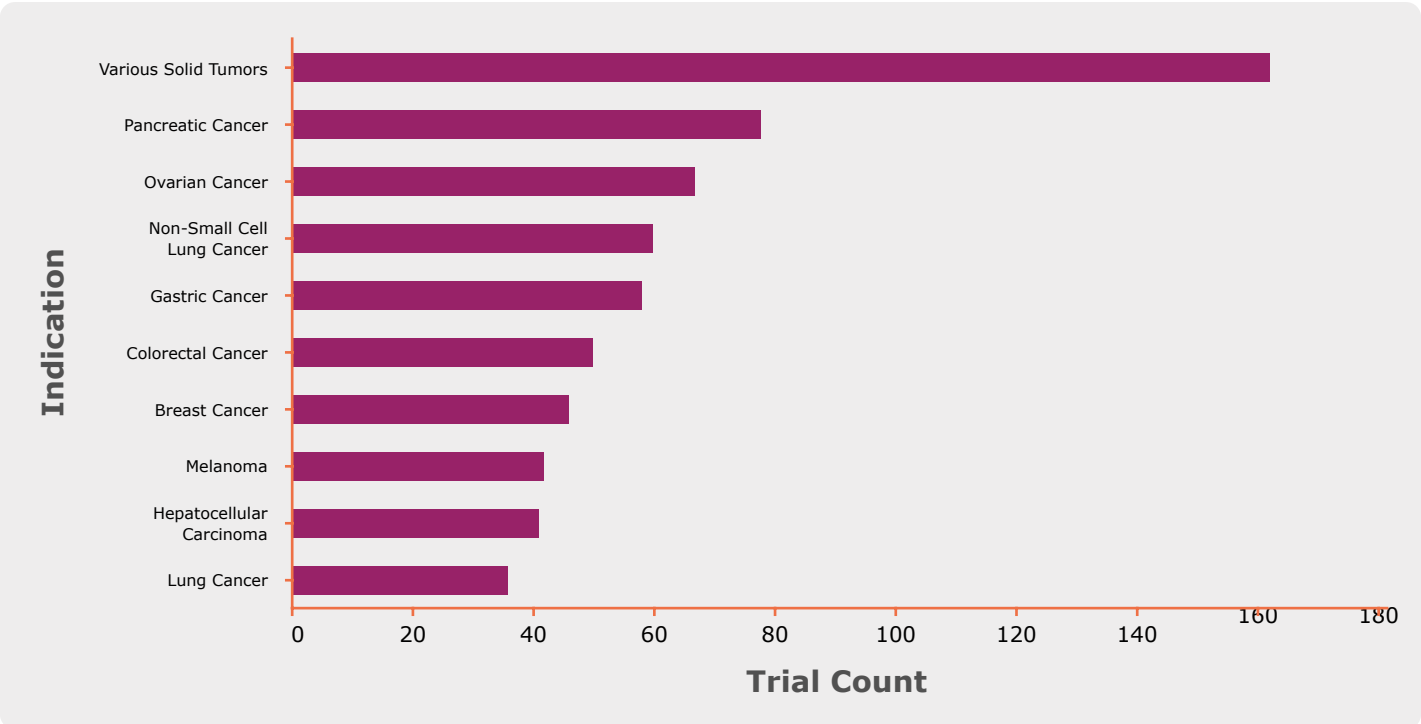
The clinical trial landscape across liquid-tumor **(Box 2)** and solid-tumor **(Box 3)** indications is also robust.[3] Where information on liquid-tumor trials has been disclosed, autologous approaches are predominant across all trial phases, roughly 80% feature CAR-T cells (followed by CAR-NK cells at ~7%), and CD19 remains the most common target (followed by BCMA and bi-specific targets). For solid-tumor clinical trials, autologous approaches remain most common, though greater diversity exists within cell types being studied (CAR-T at ~41%, followed by TILs, dendritic cells and TCR-T at 9-15% each).

Box 2. Liquid-tumor indications being explored in clinical trials as of December 2024



Source: GlobalData.[3]

Box 3. Solid-tumor indications being explored in clinical trials as of December 2024



Source: GlobalData.[3]

Robust patient responses and curative potential

The desire to improve patient outcomes lies at the heart of the cell-based IO industry. As the first adoptive cell therapies introduced into the oncology space, autologous CAR T-cell products have been delivered to roughly 40,000 patients, largely within hematology indications.[4] Clinicians now feel it is appropriate to use the term "cure", at least for many recipients of CAR-T cells who have achieved long-term remissions of previously highly refractory disease.[5] In other cases, CAR T-cell therapies have allowed for a treatment-free interval,[5] giving patients back substantial control of their lives and offering a chance for improved QoL. Success stories abound.[6-8]

Expanded access to treatment centers

To reach all patients in need, access to cell-based IO must extend beyond inpatient administration at large academic centers and/or regional centers of excellence. The University of Pennsylvania has administered over 1400 CAR-T products to date (beginning in 2010), with the majority of doses being delivered in an outpatient setting. Advantages of outpatient management are numerous[9]:

- Increased patient satisfaction and convenience
- Improved patient QoL
- Conserved inpatient resources
- Potential for improved medical care in home environment and with focused care team
- Potential for improved financial sustainability

With carefully structured outpatient programs and patient/therapy selection, ambulatory administration and monitoring for select patients can be safe, convenient, less costly, and yield similar (or perhaps even improved) patient outcomes to those observed in inpatient settings and clinical trials.[9-11]

Incorporation of community practices and community hospitals is also central to expanding patient access to cell-based IO, both from initial-infusion and follow-up standpoints. The University of Pennsylvania has successfully engaged and helped train community practices to deliver CAR T-cell therapy. Several patients treated at these community sites relayed that they would have refused treatment if extensive travel to the major, urban academic center had been required. Ensuring that patients can receive appropriate initial and follow-up care at a local facility helps to secure access to these potentially life-saving therapies for patients who may not want to, or cannot, travel to the core sites. Additional insights on outpatient and community-based access to adoptive cell therapies is found in the '***Expanding administration and care locations***' section later in the whitepaper.

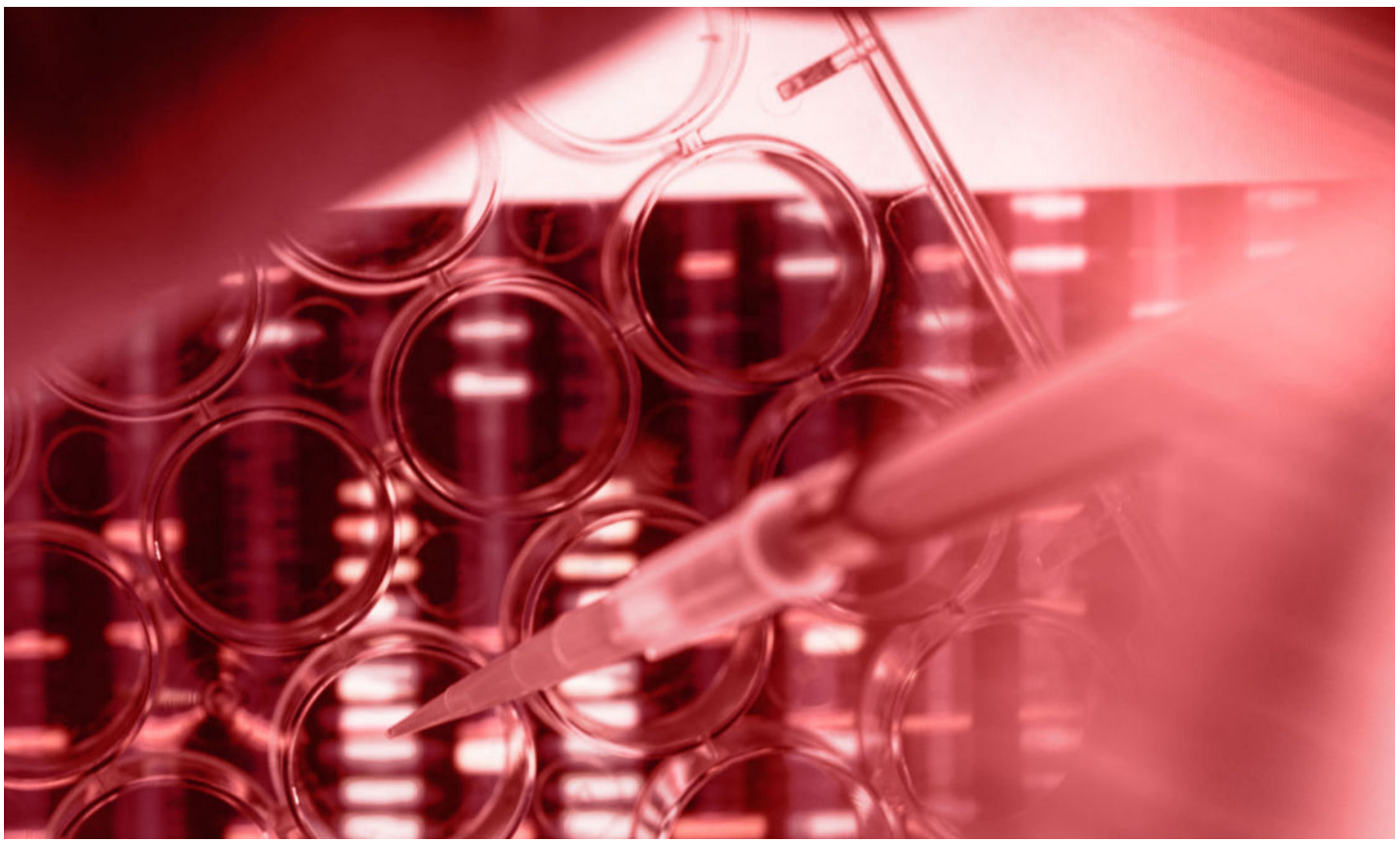
Recent regulatory advances

Regulatory advances and opportunities for cell-based IO are growing internationally, reflecting broad optimism for the field. In the United States, the recently passed PDUFA VII (2022) package allocated significant resources for FDA initiatives and staff dedicated to CGTs.[12] In addition to plans for specific guidance (see section on '***Regulatory considerations***' later in the whitepaper), the industry continues to see more opportunities for FDA engagement beyond statutorily mandated workshops, guidance, and initiatives. These include 2 pilot programs:

01 the CMC–Development Readiness Pilot (CDRP),[13] intended to facilitate CMC readiness for CBER- and CDER-regulated products with accelerated clinical development timelines; and

02 the Collaboration on Gene Therapies (CoGenT) Global Pilot, creating potential for concurrent collaborative review of gene therapy products across global regulators (first announced on January 8, 2024, at ARM's Cell & Gene Therapy State of the Industry Briefing in San Francisco[14]).

In addition, two novel designations, the Advanced Manufacturing Technologies Designation, and the Platform Technologies Designation were presented in Draft Guidance in late 2023 and 2024, respectively **(Box 4)**, and the latter was finalized in December 2024.[15,16] Each of these have significant implications for streamlining manufacturing and increasing CGT development capacity.



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Any questions about ARM membership or accessing our community portal can be sent to: member@alliancerm.org

If you are not an ARM member but would still like to read the whitepaper, access can be purchased through the link here: https://alliancerm.wufoo.com/forms/mtt6y771qqsiq1/