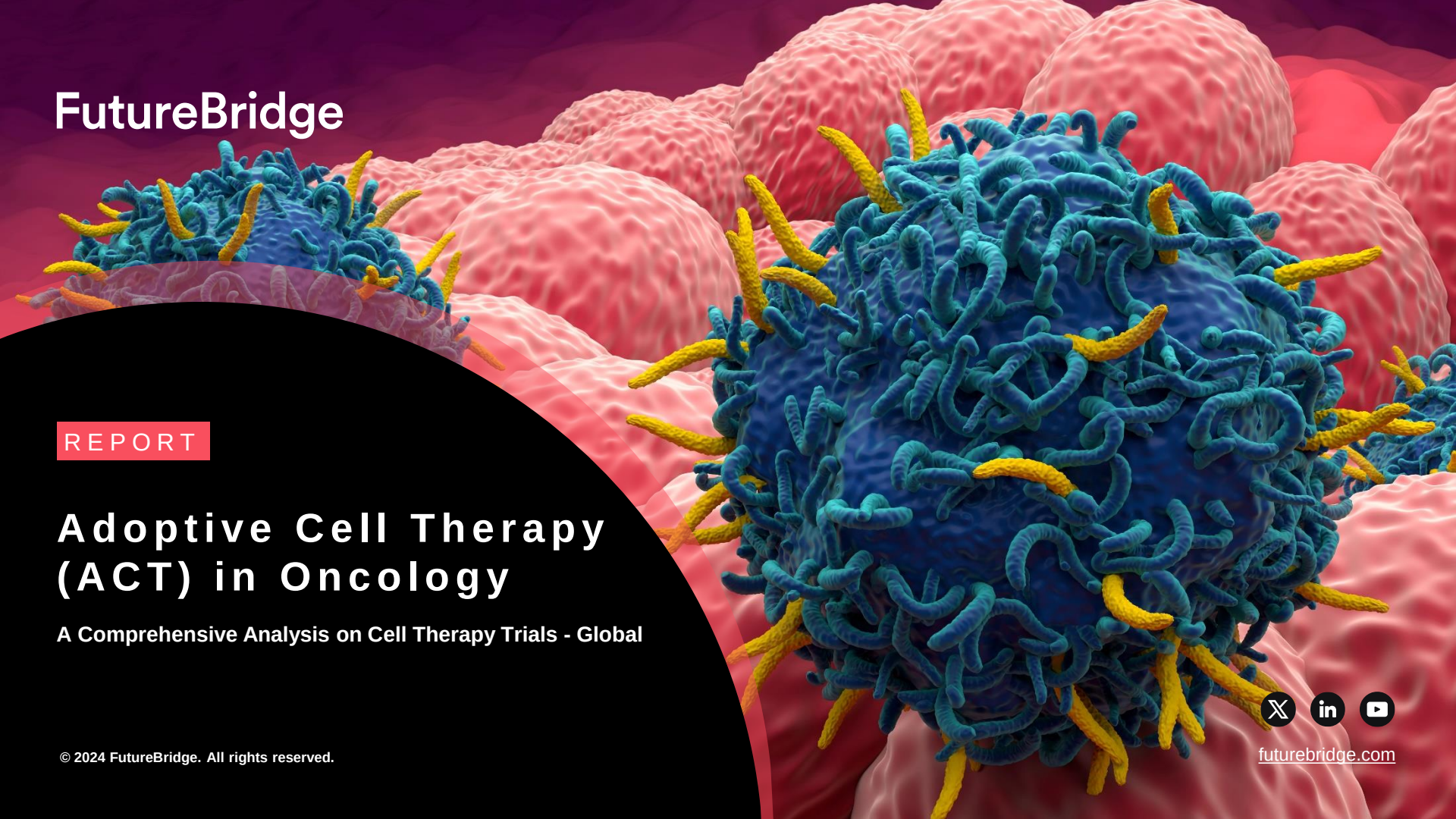
FutureBridge

REPORT

Adoptive Cell Therapy (ACT) in Oncology

A Comprehensive Analysis on Cell Therapy Trials - Global



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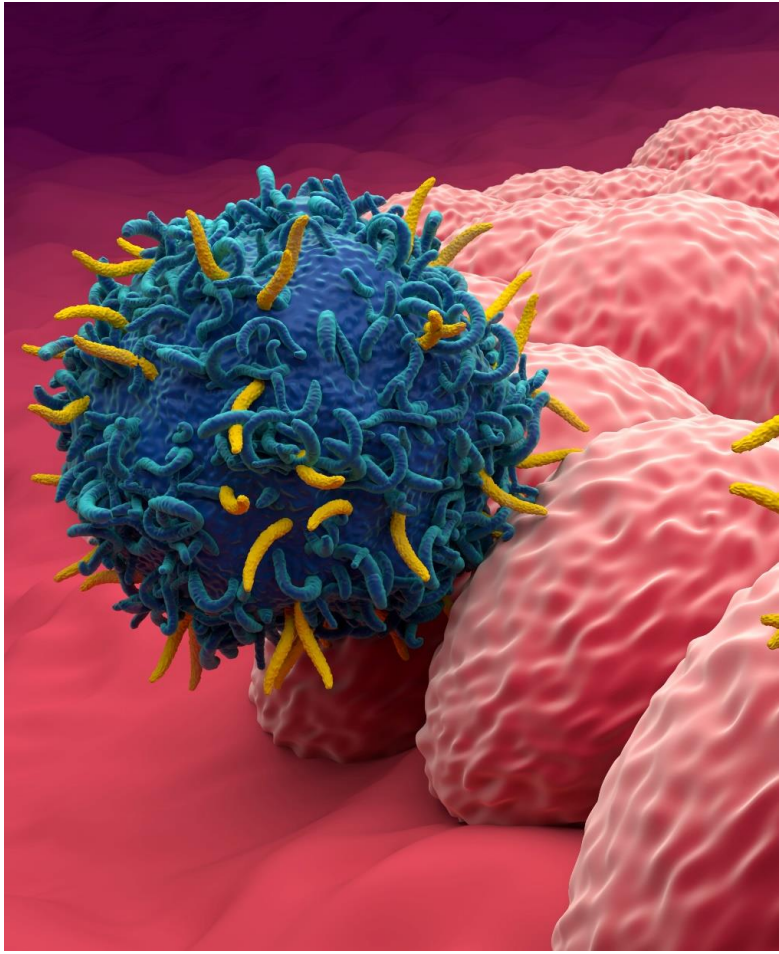


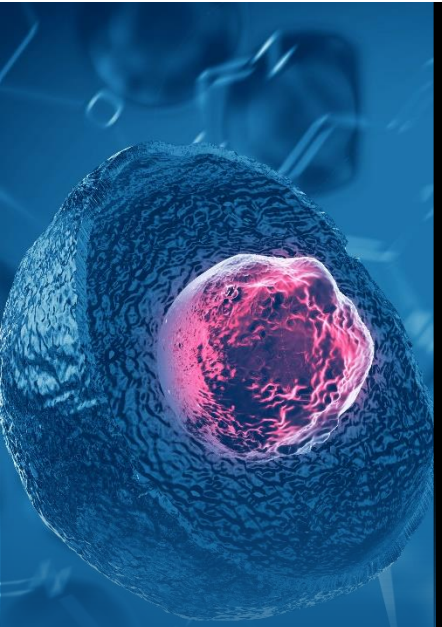
List of Abbreviations

Acronym	Definition
ACT	Adoptive Cellular Therapy
ACTR	Antibody-coupled T Cell Receptor
ALK	Anaplastic Lymphoma Kinase
BCMA	B Cell Maturation Antigen
BTK	Bruton Tyrosine Kinase
CAGR	Compound Annual Growth Rate
CAR	Chimeric Antigen Receptor
CEA	Carcinoembryonic Antigen
CEACAM5	CEA Cell Adhesion Molecule 5
CIK	Cytokine-induced Killer
CIML	Cytokine-induced Memory-like
CIR	Chimeric Immune Receptor
CTL	Cytotoxic T Lymphocytes
CTLA-4	Cytotoxic T-lymphocyte Associated Protein 4
DART	Dual-affinity Re-targeting
DC vac	Dendritic Cell Vaccines
EBVST	Epstein-Barr Virus-Specific T Cells
EGFR	Epidermal Growth Factor Receptor
EpCAM	Epithelial Cellular Adhesion Molecule
GPC3	Glypican 3
HEKT	Human Embryonic Kidney T Cell

Acronym	Definition
HER2	Human Epidermal Growth Factor Receptor 2
HSCT	Haematopoietic Stem Cell Transplantation
ICI	Immune Checkpoint Inhibitors
ICT	Integrated Circuit T Cell Therapy
IgT	Immunogene-modified T
IMiD	Immunomodulatory Drug
IO	Immuno-oncology Or Immunotherapy
KEAP1	Kelch Like ECH Associated Protein 1
mAb	Monoclonal Antibody
METi	Mesenchymal Epithelial Transition Factor Receptor Inhibitors
MIL	Marrow Infiltrating Lymphocytes
MUC1	Mucin 1
NA	Not Available
Nab-P	Nab-paclitaxel
NK	Natural Killer Cell
NKG2D	Natural Killer Group 2 Member D
NSCLC	Non-Small Cell Lung Cancer
NY ESO-1	New York Esophageal Squamous Cell Carcinoma 1
ORR	Overall Response Rate
PCL	Plasma Cell Leukemia
PD-1i	Programmed Cell Death Protein 1 Inhibitor

Acronym	Definition
PD-L1i	Programmed Death Ligand 1 Inhibitor
PNK	Primary Natural Killer
Rivo-cel	Rivogenlecleucel
R&D	Research And Development
R/R	Relapsed/Refractory
ROS1	ROS Proto-oncogene 1
SoC	Standard of Care
STAR-T	Synthetic TCR And Antigen Receptor T Cell
TAA	Tumor Associated Antigen
TAAT	Tumor multi-Antigen Associated -specific cytotoxic T lymphocytes
TACT	T-cell Antigen Coupler T Cell
Tcm	Central Memory T Cell
TCR	T-cell Receptor
TIGITi	T-cell Immunoglobulin And ITIM Domain Inhibitor
TIL	Tumor-infiltrating Lymphocytes
Tisa-cel	Tisagenlecleucel
TKI	Tyrosine Kinase Inhibitor
Treg	T Regulatory Cell
US	United States
USD	United States Dollar

ACT is a Game-changer Due to Its Clinical Promises that Address the Most Complex Unmet Needs



Analysis and Insights of the ACT Clinical Landscape, R&D Trends, Key Technologies, Collaborations, & Investments

This report encompasses several key components, like:

- Therapeutic Targets (~335)
- Indications (~304)
- Novel Platforms
- Competitive Landscape
- Trial Progression
- Player Ecosystem
- Geographic Spread
- M&A, Licensing and Strategic Partnerships

ACTs are effectively treating heme & solid cancer patients who are/have:

- Limited Treatment Options
- Refractory or Progressive Disease
- High Unmet Need
- Immunologically Cold Tumors
- Novel Targets Lacking Any Targeted Therapy

Clinical Landscape Coverage Demographics

2400+
Active Oncology Clinical Trials

350+
Corporate Entities

1450+
Heme Malignancies Clinical Trials

980+
Solid Tumors Clinical Trials

15
Cell Therapies Approved

Types of ACT Covered In The Report

- CAR T-cells including CAR γδ-T, CAR-DC Vaccine, CAR EBVST, etc
- NK cells including CAR-NK, NKT, CIML-NK, PNK, SMT-NK
- TILs, CAR TILs, MILs, CTLs
- TCR, ACTR
- Macrophage, CAR Macrophage
- Cytokine-induced killer cell therapy
- Other ACTs including γδ T, Memory T cells, Treg, Ig T, Tcm cells, TAC T cells etc.

Impressive Growth of 7.5X is Expected in ACTs (Oncology) - $36.6 Bn from $4.8 Bn (2033 vs 2023)

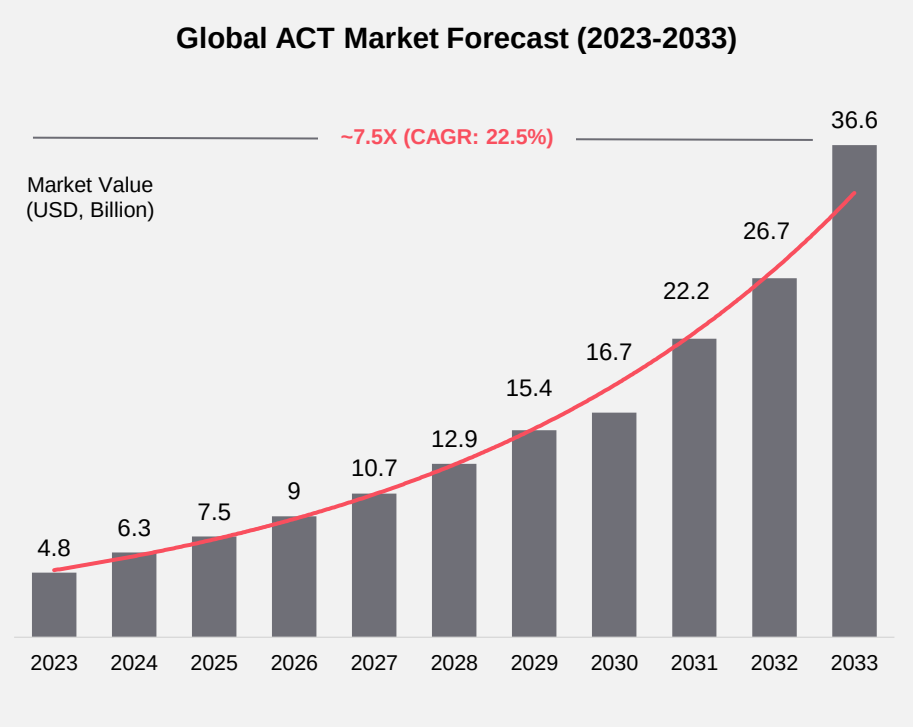
36.6 USD billion market is expected by 2033

22.5% CAGR is expected from 2023-2033

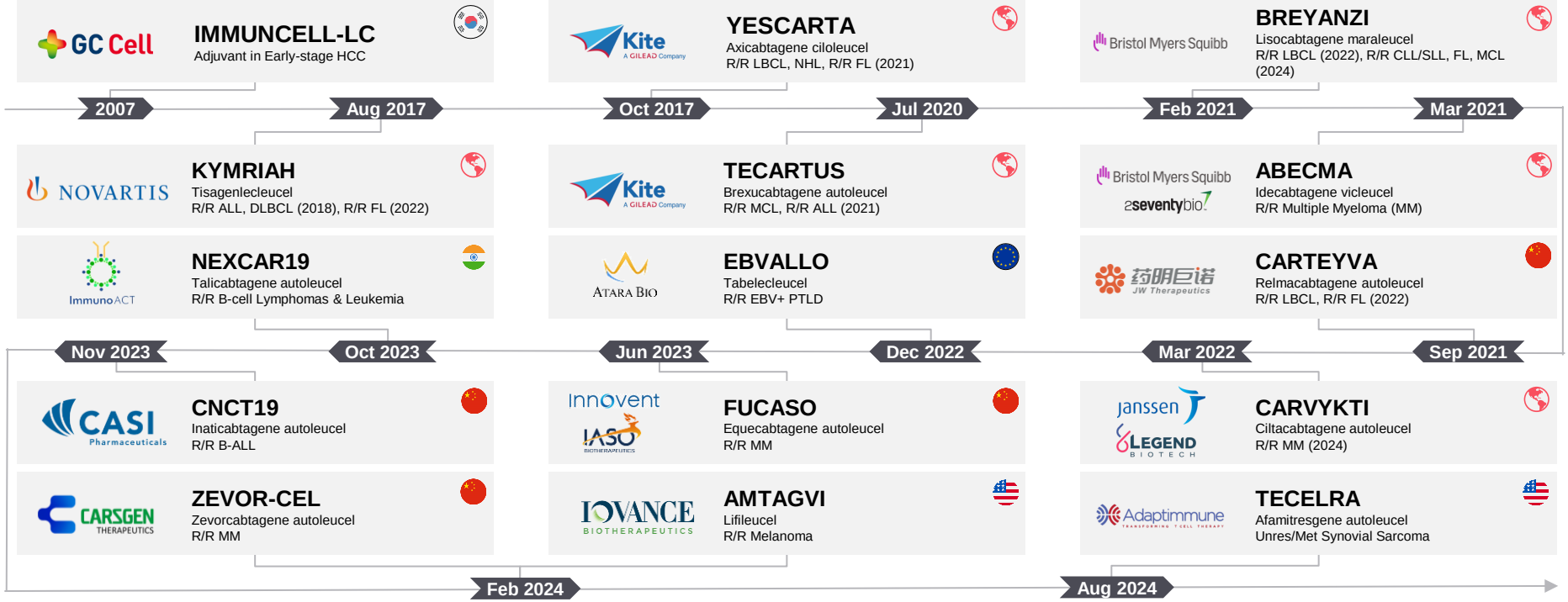
~60% Trials are in early phase indicates massive growth in upcoming years

>700 Industry & academia players would disrupt the cancer market

~60% Autologous ACTs clinical trials under clinical development



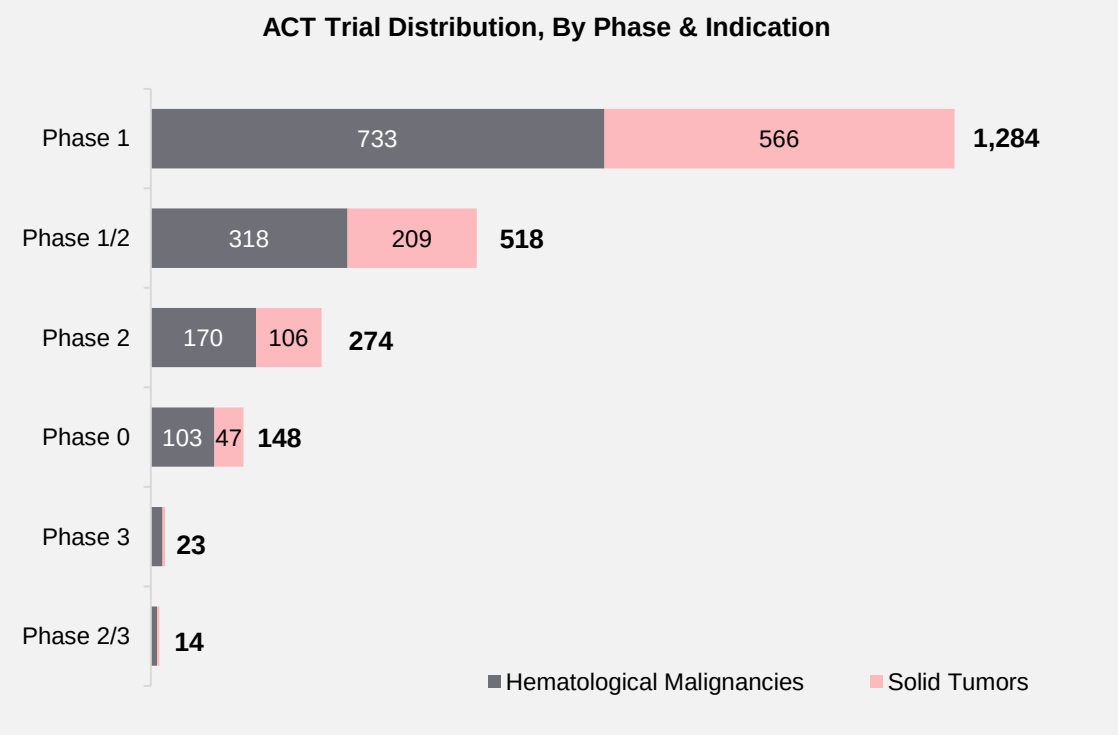
ACT Approval Timeline – Global



Indicates Approval in Major geographies such as US, EU, Japan & China; Presented logos and Trademarks belong to the respective entities

Abbreviations: HCC - Hepatocellular carcinoma; R/R – Relapsed Refractory; Unres/Met – Unresectable, Metastatic; LBCL - Large B-cell Lymphoma; NHL – Non-Hodgkin lymphoma; ALL – Acute Lymphoblastic Leukemia; CLL – Chronic Lymphocytic Leukemia; DLBCL – Diffuse Large B-cell Lymphoma; FL – Follicular Lymphoma; SLL – Small Lymphocytic Lymphoma; MCL - Mantle cell lymphoma; PTLD - Post-transplant Lymphoproliferative Disorder

Recent Regulatory Approvals in Solid Tumors are likely to Boost the Industry Confidence and Clinical Trial Activity



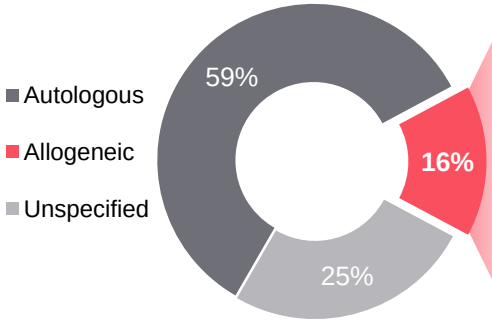
Hematological malignancies remain dominant in across trial phase, but recent regulatory successes with ACTs for solid tumors reflects growing optimism for ACTs' potential beyond hematologic cancers

- Majority of trials are in phase 1, followed by Phase 1/2, with a greater focus on hematologic cancers over solid tumors
- Among 2,390 ongoing ACT trials, only 13% are in phase 2 or phase 3

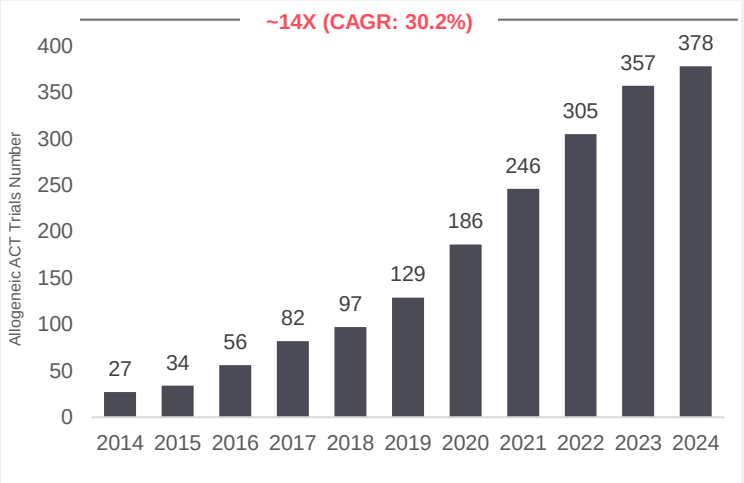
Note: Around #129 Trials without available phase information are not considered; All phase 0 trials are registered trials in China only.

Allogeneic Therapies being 'Off-the-shelf' are Gaining Traction and likely to be Highly Scalable with Consistent Batch Production

ACT Trial Distribution, By Cell Source



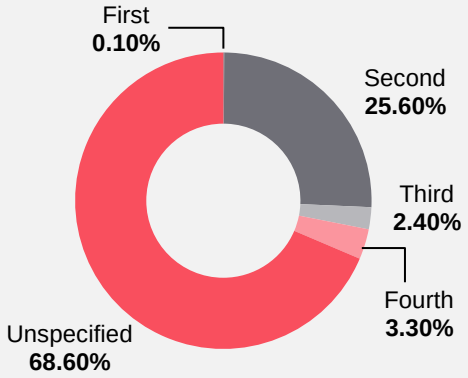
Allogeneic ACT Trials Incremental Trends (2014-2024)



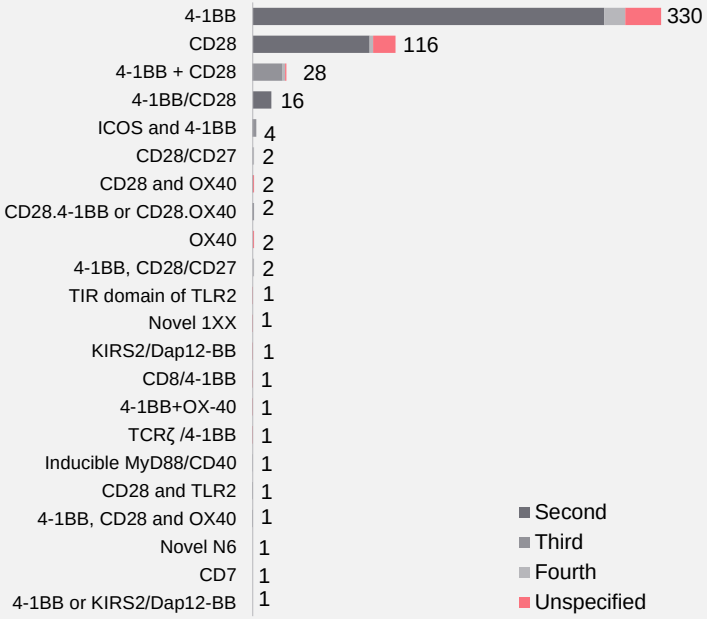
- Autologous therapies currently lead the field, but allogeneic therapies are rapidly gaining traction, signaling a diversification in cell therapy approaches
- The notable rise in allogeneic therapies indicates growing confidence in their potential, driven by technological advances, off-the-shelf availability, and enhanced safety and efficacy

Evolution in CAR Constructs hold a Great Promise for an Improved Efficacy and Accessibility

ACT Trials Distribution, By CAR Generation



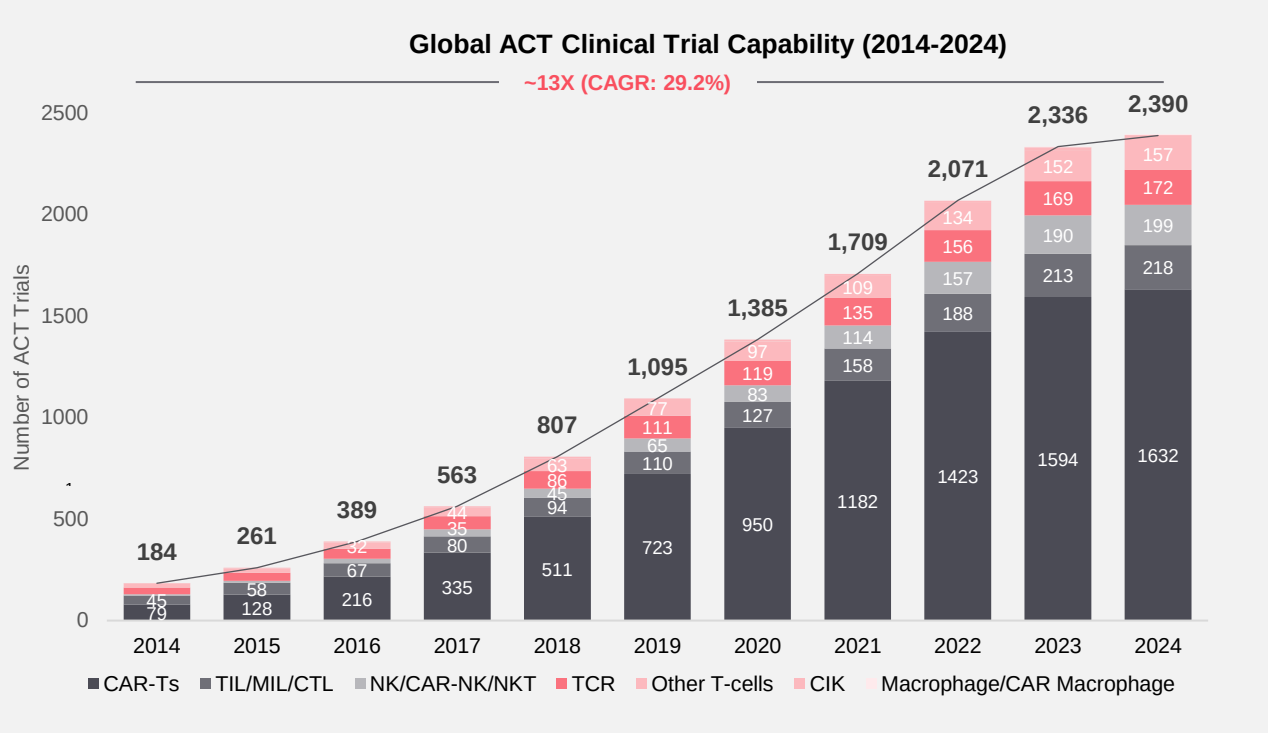
ACT Trials Distribution, By Generation & Co-stimulants Type*



- While many ACT generations remain undisclosed, 2nd generation ACTs are the most common among those reported.
- Fourth-generation ACTs, which secrete universal cytokines such as IFN-γ, TNF-α, IL-2, and IL-8, are emerging as promising due to their potential to reduce systemic toxicity while enhancing tumor targeting and immune cell recruitment
- Trials predominantly favor the use of 4-1BB and CD28 co-stimulatory molecules to boost cell persistence and antitumor efficacy

Clinical Trials have been continuously Growing, Reflecting a High Intent, R&D Activity and Investments

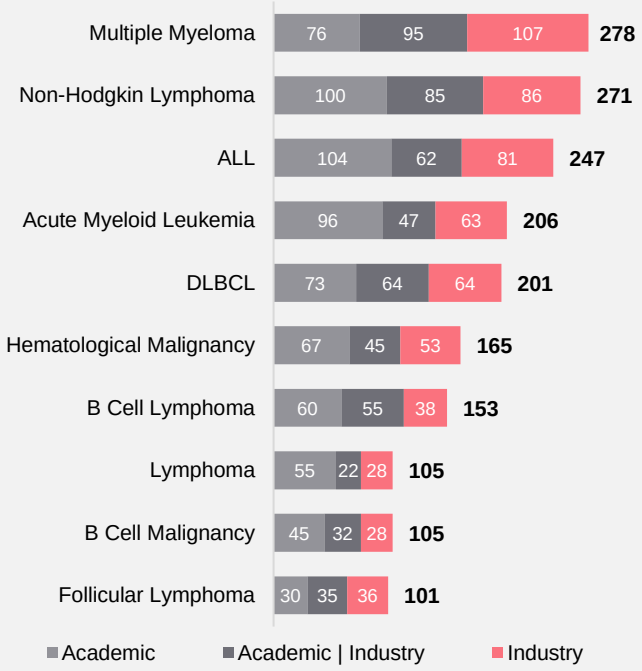
- The past few years have witnessed a significant expansion in the number of registered clinical trials
- In 2024, out of the 2,390 ACT trials initiated globally, CAR T-cell therapy emerged as the dominant approach, accounting for approximately 68% of trials. This is followed by TILs (9%), underscoring their growing role in clinical development.



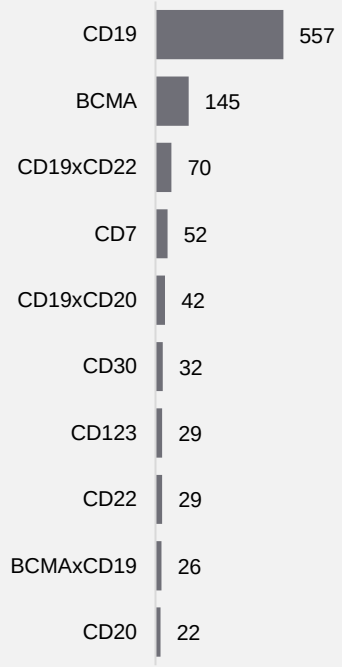
Note: Other T-cells include – CIR T-cell, Gamma delta T-cell, HEKT-cell, ICT-cell, Ig T-cell, Memory T-cell, TAC T-cell, Tcm cell, Treg cell

ACT has Transformative Potential which is evident through Multiple Approvals In Heme Malignancies

ACT Trial Distribution in Hematological Malignancies



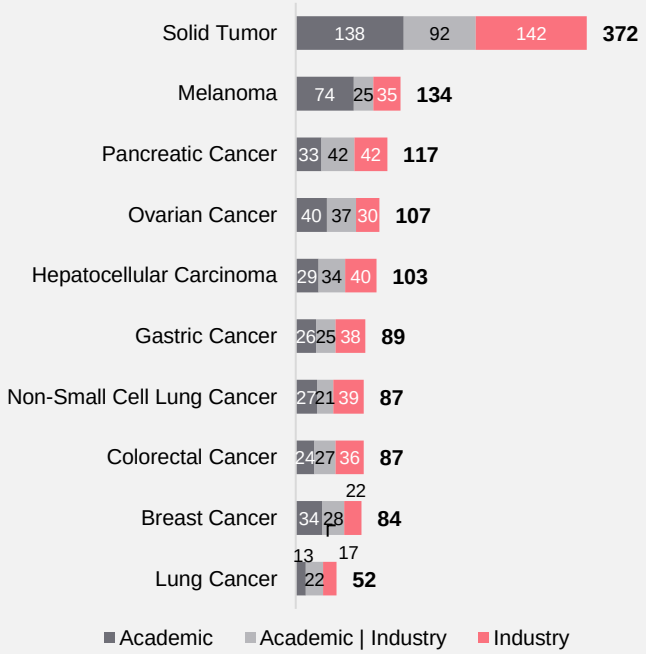
ACT Trial Distribution By Biomarker in Hematological Malignancies



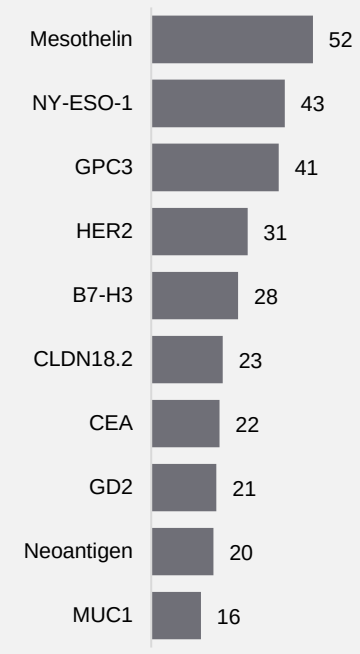
- Cell therapies are well-established for hematological indications with multiple approvals, however, ongoing efforts are needed to address the existing challenges
- The industry's focus on multiple myeloma (MM) is evident, with numerous BCMA-targeting cell therapies under development
- Significant pipeline activity is also underway for NHL, ALL, AML, and DLBCL

With the recent two approvals of ACTs in Solid Tumor, the field is Gaining Momentum

ACT Trial Distribution in Solid Tumors

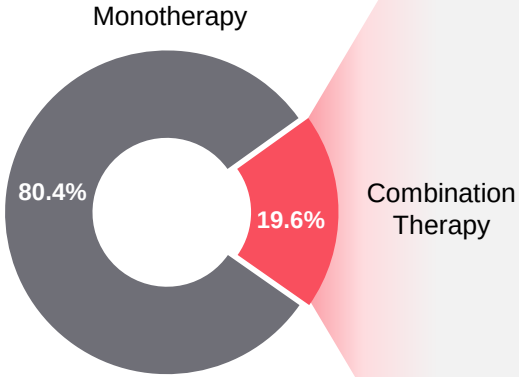


ACT Trial Distribution By Biomarker in Solid Tumors

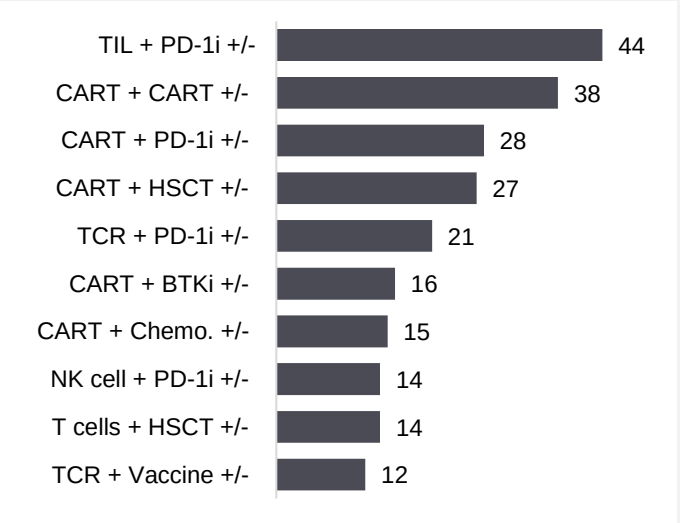


- Cell therapies are being rigorously tested in basket and umbrella trials for solid tumors
- Following significant progress in cell therapy, the leading solid tumors with the highest clinical trial activity are
  - Melanoma
  - Pancreatic Cancer
  - Ovarian Cancer
  - Hepatocellular cancer
- Mesothelin, NY-ESO-1, GPC3, are major tumor antigens targeted by cell therapy trials; Emerging targets like EpCAM, NKG2D enhance tumor specificity and immune response by engaging NK and T-cells

Combining ACTs with SoC has opened Promising New Avenues for more Successful Treatment



ACTs Combination Trial Distribution*



Coupling cell therapy with other approaches like ICI, HSCT & BTKi is under intense investigation and offers significant benefits, such as:

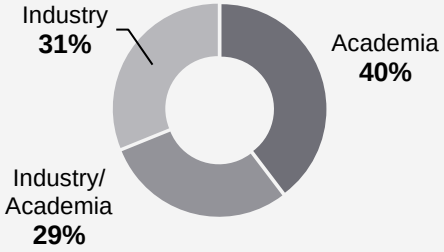
- Enhanced treatment efficacy
- Overcome resistance
- Improved safety and tolerability
- Broad tumor eradication
- Expanded applicability

Of the total 2,390 cell therapy trials, about ~20% focus on cell therapy combination therapies with major partners including PD-1i, CAR-T, chemotherapy, transplant, and small molecule

*Note: Only the top 10 combination therapies are listed, ranked by the number of clinical trials; '+/-' indicates that the combination regimen may or may not contains more than 2 combination partners

Breakthrough Innovations in ACTs are contributed by Both Industry and Academia

- Of the total 2,390 ACT trials, ~31% of them are sponsored solely by pharmaceutical companies
- Globally, around 450 industries and 550 academic institutions have assets in the clinical pipeline, distributed as follows:
  - 222 companies are focussed on hematological malignancies
  - 227 are targeting solid tumors
- Key players with Phase 3 ACT assets in development include Novartis, Janssen, BMS, Kite Pharma, Adaptimmune, Iovance, GC Cell Corp, Tessa Therapeutics, Sorrento, Wuhan Sian Med Tech, Bellicum, and Orca Biosystems.



Key Players With ACT Assets Under Clinical Development

NOVARTIS
janssen
Bristol Myers Squibb
Adaptimmune
TRANSFORMING T CELL THERAPY
IOVANCE
BIOTHERAPEUTICS
Kite
A GILEAD Company
ATARA BIO
TESSA
THERAPEUTICS
orcabio
Bellicum
药明巨诺
JW Therapeutics
GC Cell
sorrento
THERAPEUTICS
SIAN思安
Wuhan Sian Medical Technology
UNI-CAR
优卡迪
ImmunityBio
LEGEND
BIOTECH
BIONTECH

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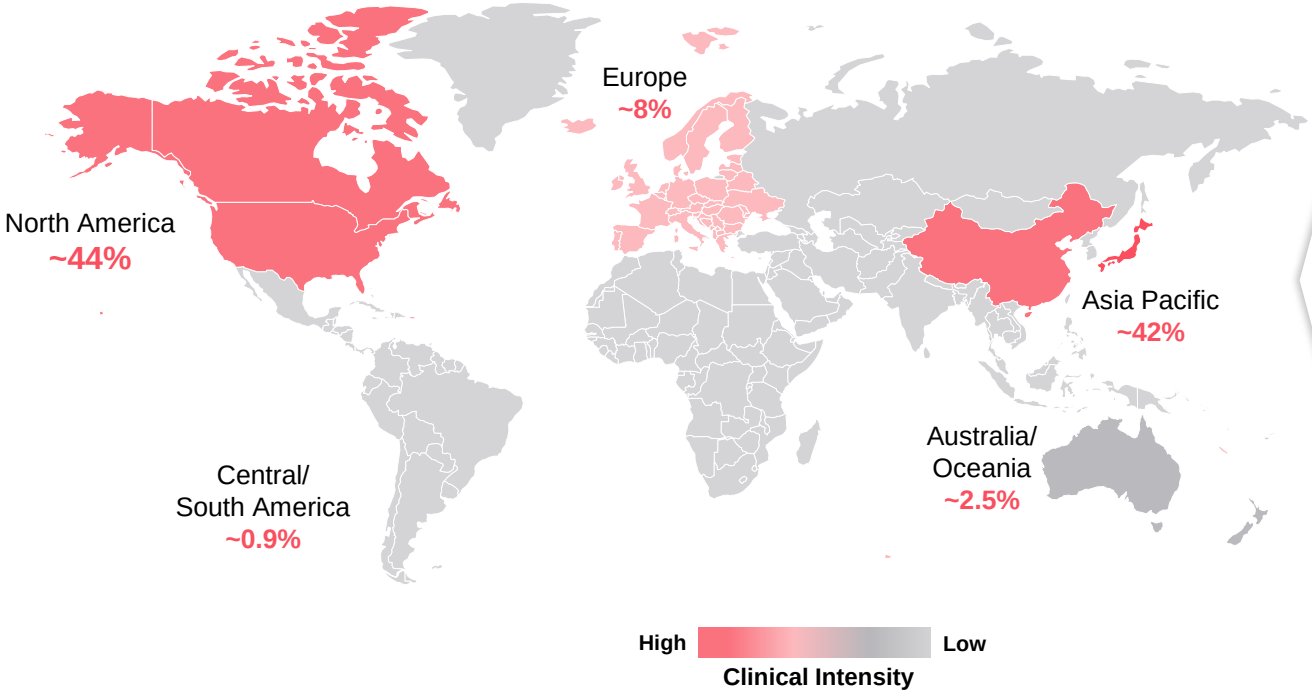
China Leads the Market, Followed by USA – Jointly they contribute ~80% of the ACT Clinical Trials

Geographical Distribution of ACT Trials



- China leads the global ACT landscape with **1,292** clinical trials, followed by the USA with **790** trials
- The USA is placing a growing emphasis on advanced cell therapy approaches, with **~50%** of its trials dedicated to exploring innovative treatments such as TILs, TCR therapies, NK cells, and other emerging cell therapies

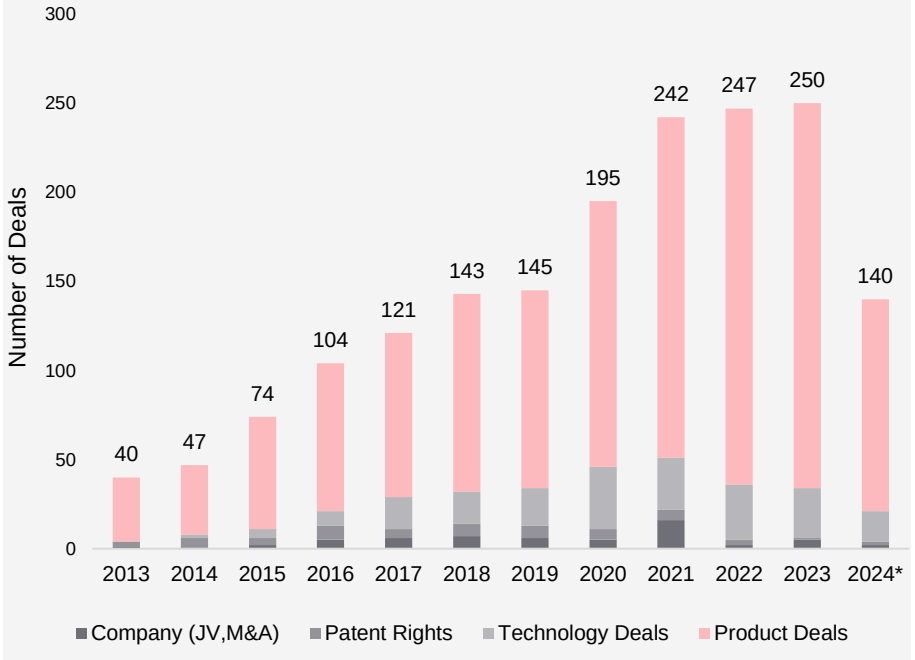
Summary of Key Novel CAR Platform: Boosting Speed, Precision, Safety, & Accessibility Through Innovation

Company	Asset	Platform	Cell Source	Indication	Phase	Vein-to-vein time	Manufacturing time
NOVARTIS	**Durcabtagene autoleucel (PHE885)**	T-Charge	Autologous	MM	2	≤10 days	<2 days
Adaptimmune	**Uzatresgene autoleucel (ADP-A2M4CD8)**	SPEAR	Autologous	Ovarian Cancer	2	17-24 days	12 days
MARKER Therapeutics	**Zedenoleucel (MT-401)**	Multi-TAA technology	Allogeneic	AML	2	Off-the-shelf	9 days
AstraZeneca GRACELL	**AZD0120 (GC012F)**	FasTCAR	Autologous	MM	1/2	NA	22-36 hours
Allogene THERAPEUTICS	**ALLO-605**	TurboCAR	Allogeneic	MM	1/2	Off-the-shelf	NA
CARSGEN THERAPEUTICS	**CT071**	CARcelerate	Autologous	MM, PCL	1	18-44 days	<2 days
AVENCELL	**AVC-201**	Universal switchable CAR	Allogeneic	AML	1	Off-the-shelf	NA

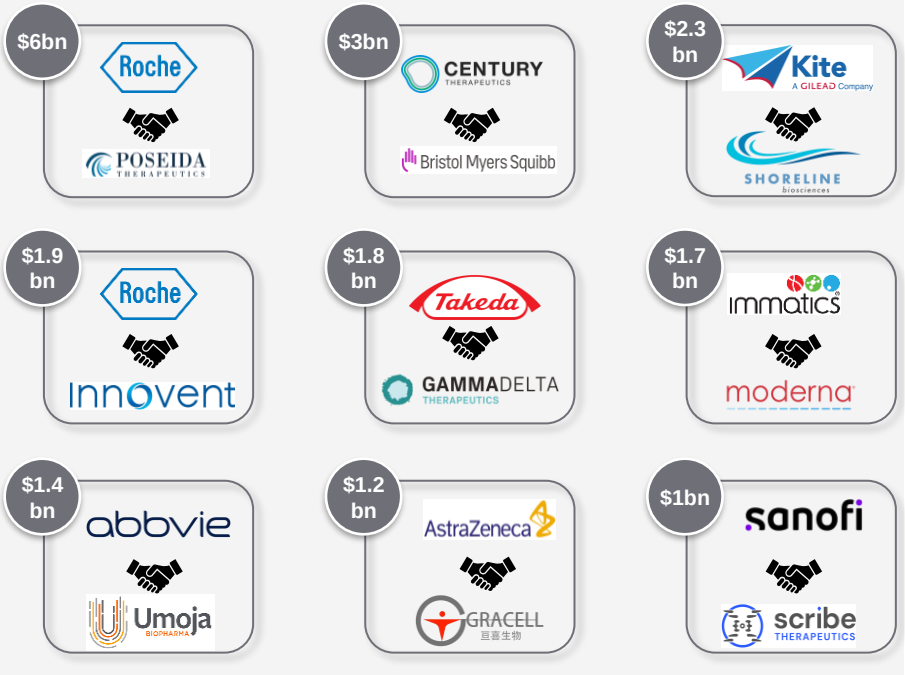
NOTE: The platforms mentioned here are specific to the given asset and its corresponding indication

Multibillion-Dollar Deals Propel Remarkable Growth in ACTs Development

M&A activity trends in Oncology ACT space



Featured Deals (>$1Billion) from the Past 5 years



*Based on available data till August 2024; Abbreviations: JV- Joint-Ventures; M&A- Merger & Acquisitions; Presented logos and Trademarks belong to the respective entities

# Indicates highest projected values

ACT market is Crowded and there is a strong competition between US and Chinese Entities

Academia

City of Hope
Memorial Sloan Kettering Cancer Center
NIH National Cancer Institute
中山大學 Sun Yat-sen University
浙江大學 Zhejiang University
Fudan University
Moffitt Cancer Center
UCL
北京大學 Peking University
Herlev Hospital
Penn
BCM Baylor College of Medicine
UNC Lineberger Comprehensive Cancer Center

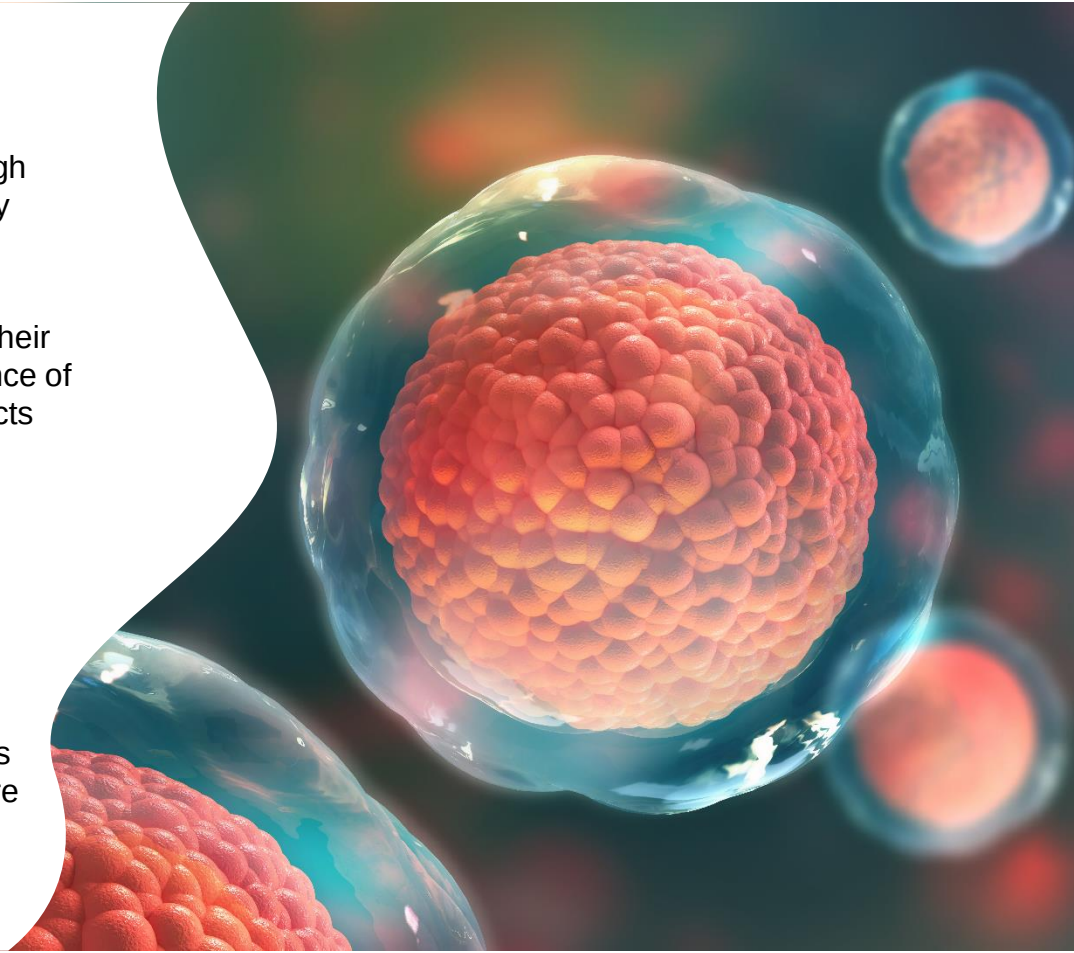
Start-ups & SMEs

nkarta
Adicet Bio
carisma therapeutics
Fate Therapeutics
MARKER Therapeutics
Celyad Oncology
AVENCELL
优卡迪
innovent
TESSA Therapeutics
IASO Biotherapeutics
ATARA BIO
CASI Pharmaceuticals
ImmunoACT
2seventybio
Bellicum
SIAN思安 Wuhan Sian Medical Technology

Established Players

Bristol Myers Squibb
NOVARTIS
Kite A GILEAD Company
AstraZeneca
GC Cell
janssen
药明巨诺 JW Therapeutics
IOVANCE BIOTHERAPEUTICS
LEGEND BIOTECH
Adaptimmune TRANSFORMING T CELL THERAPY
abbvie
BIONTECH
ImmunityBio
Takeda

- Cell therapy pipeline is rapidly evolving and diversifying, with a projected **CAGR of 22.5%** through 2030, driving therapeutic advancements in Oncology
- Cell therapies have become market leaders due to their potential for long-term responses and the convenience of being '***off-the-shelf***' and '***one-time infusion***' products
- Future of **cell therapies is propelled** by advancements in technology, improvements in manufacturing, and strategic commercialization
- **Collaboration** coupled with increased investment, is crucial to unlock the cell therapy potential and ensure its long-term success



Methodology – Sources and Scope

Secondary Research Methodology

Pipeline and Trial Data

- Data was obtained from clinical trial registries such as ClinicalTrials.gov, the EU Clinical Trials Register, ICTRP, and CHICTR, among others
  - The analysis covered various parameters, including registration year, patient population, trial status, phase, sponsor type, patient segment, study design, leading players, and geographical distribution
  - The scope included cell therapies such as CAR-T, NK cells, TCR, TILs, gamma delta T-cells, and other cell therapies
  - All academic trials, company-sponsored trials, and collaborations between companies and academia were included
  - No trials were excluded based on trial status
- The time frame for the data collection was from January 2014 to April 2024
- A paid database was used to cross-check all cell therapy products included in the final database

Market and M&A (Deals) Data

- The report includes the market value for the base year 2023 and provides annual revenue forecasts through 2030
- It offers a brief analysis of recent partnerships in cell-based therapies, covering aspects such as partnership type, deals number, & leading players

Clinical Trial Registries

ClinicalTrials.gov
International Clinical Trials Registry Platform Search Portal
ChiCTR
EU Clinical Trials Register
jRCT Japan Registry of Clinical Trials

Scientific Literature

PubMed
Scopus
LENS.ORG
nature
blood
CANCER RESEARCH UK
AACR American Association for Cancer Research
NIH NATIONAL CANCER INSTITUTE

Paid Databases & Conferences Covered

Cortellis™ A Clarivate Analytics solution
Adis Insight
ASCO
ESMO
American Society of Hematology

FutureBridge Expertise can help you Track and Outperform Competitors with Custom Intelligence

Our Industry Veteran Experts Can Help You !

- Navigate threats, changing market regulations and emerging competition
- Identify white spaces and expansion opportunities
- Collaborate/partner with prioritized synergistic opportunities
- Identify disruptive emerging technologies
- Benchmark your asset against competitors

Thank you

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