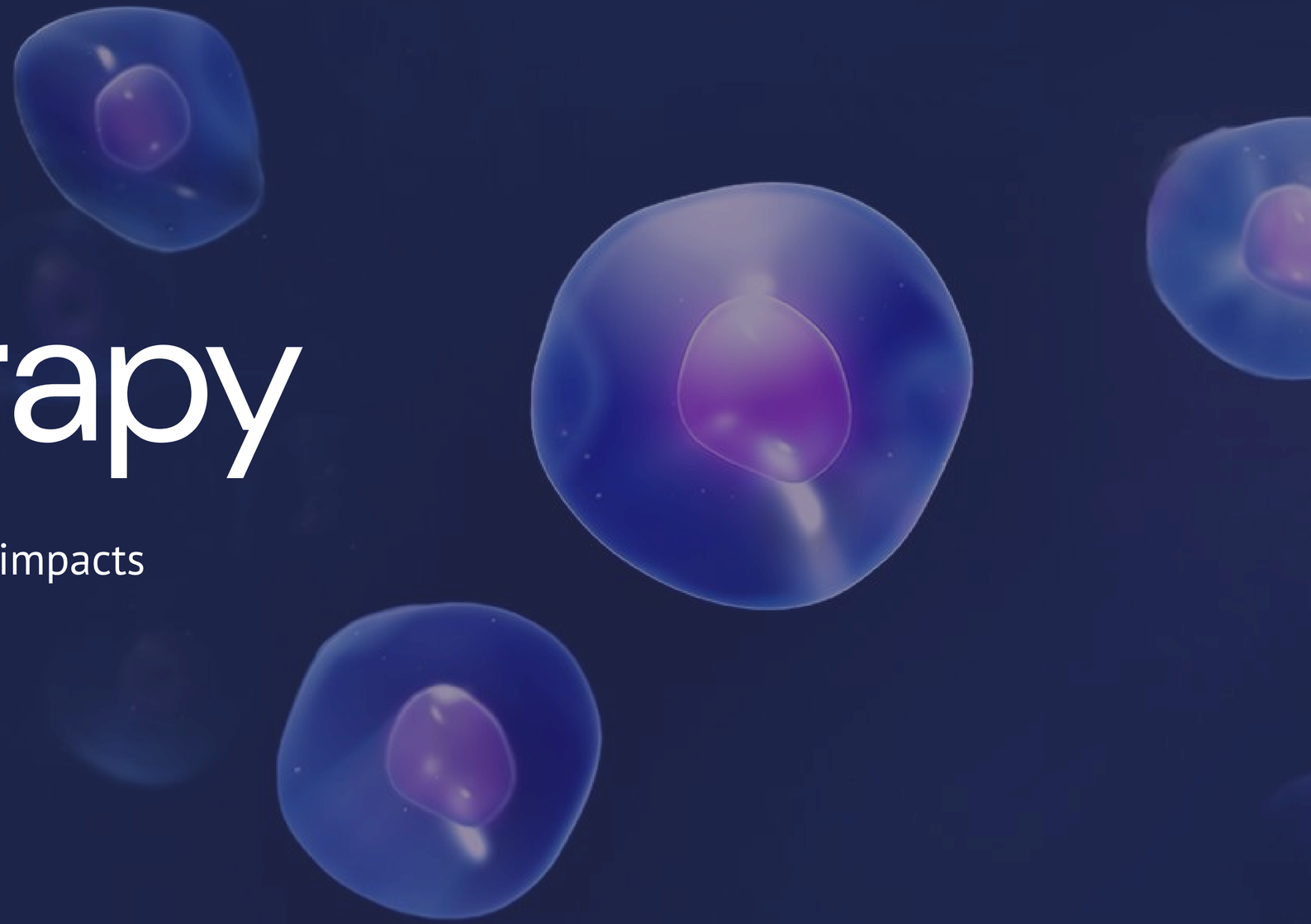
Cell Therapy

Microscopic treatments making big impacts



Agenda

Overview

Cell therapy involves **treating** disease **by administering living** cells into a patient to **repair, replace, or reprogram** malfunctioning cells.

Cell therapy harnesses patient cells for lasting cures, and a **highly personalized** and potentially **curative** treatments for a **range** of conditions

Phase 1

- Initial small trials
- **Tests safety,** dosage, and side effects

Phase 2

- Medium-scale trials
- Evaluates **efficacy** and continue monitoring

Phase 3

- Large-scale trials
- **Continuation** and **comparative** trial

Types: Source

Autologous

Patient-derived cells are **modified and re-infused**—minimizing rejection (e.g., CAR-T) but costing **~$400k** per dose and **hard to scale.**

Allogeneic

Donor cells **create off-the-shelf** products that are **scalable** and **lower-cost,** though they require some editing to manage rejection risks.

Types: Main Cell Types

Stem Cells

Uses versatile cells from sources like bone marrow to repair damaged tissues, offering **regenerative benefits** while requiring careful control for safety.

CAR-T

Uses patient's or donor's T cells **engineered to target** cancer cells and fight blood cancers, though it's costly and can have significant side effects.

Natural Killers

Natural Killer (NK) cells, from patients or donors, targets and kills cancer cells, providing an option that may **reduce** immune-related side effects.

History

Early forms of cell therapy **emerged** with procedures like bone marrow **transplants**.

1950-1970

1997

Genzyme's Carticel was FDA approved, an autologous implant for repairing knee cartilage injuries.

U.S. **policy** established the **RMAT designation**, offering **expedited FDA review** for qualifying cell therapies and gene therapies

2016

2020's

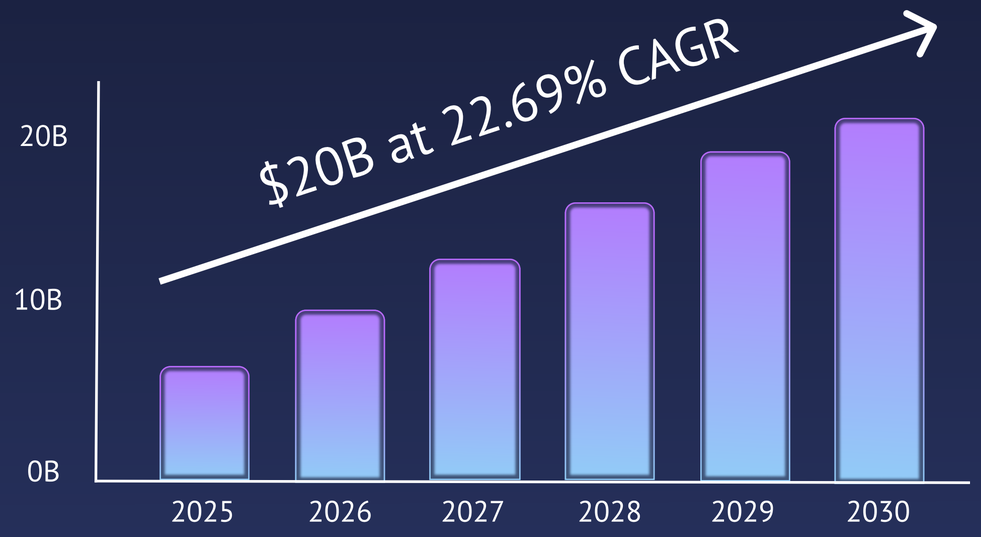
Due to COVID, there was a **spike in demand for cell therapy**. By **2023, six CAR-T** therapies were **approved** in the U.S.

Value Proposition

Different types of cell therapies and companies propose **unique values**

	Autologous	Allogeneic	CDMO	Big Pharma
+ VALUE	Personalized, no risk of rejection, low risk of GVHD, and shorter recovery time	Potential for mass production, shorter wait times, and allows for cell diversity	Provides means of development and regulatory support, increases speed-to-clinic	Offers commercial-scale means of production of therapies, as well as funding for R&D
— LIMITS	Limited scalability with high manufacturing costs and slow turnaround time	GVHD/rejection can lead to immunosuppression dependency	Not involved in treatment development which is what drives the market	Therapies acquired in earlier stages may not be successful

Market



$15.2B
Investments in cell/gene therapy (2024)

$1.94B
Go-to-market costs (2024)

77%
Rise in cancer cases from 2022 → 2024

Growth Factors

- Increasing cases of chronic diseases: Cancer, diabetes, cardiovascular, etc.
- More funding for R&D sparked by the pandemic and aging demographic
- Maturation leads to higher approvals and clearer regulatory frameworks

Market: Map

Segmented by lead candidates/main products or services

T-Cell Therapies (CAR-T, TCR, ATT)

Autologous

Autolus, Lyell, capstan therapeutics, ARCELLX, Seattle Children's, Roche, Kite A GILEAD Company, ArsenalBio, BLUEROCK, Adaptimmune

Allogeneic

kyverna, Takeda, CARIBOU BIOSCIENCES, CRISPR THERAPEUTICS, AsherBio, sanofi, Intellia THERAPEUTICS

Non T-cell (NK, TIL, Stem)

Autologous

InGeneron, VERICEL, INDAPTA THERAPEUTICS

Allogeneic

TreeFrog, nkarta, MORPHOCELL, artiva, Ossium Health, BAYER, astellas, Celyad Oncology, AFFIMED

Manufacturing & Platform-Focused

Curate BIOSCIENCES, Oxford Biomedica, Oribiotech, MINARIS, caldevron, pluri, MUSTANGBIO, MEIRAGTx, nanoString, MaxCyte, charles river, Spark, Catalent, SCORPIUS, CELLARES, AVECTAS, PRECISION, Fate THERAPEUTICS, CENTURY THERAPEUTICS, GILEAD, FUJIFILM Cellular Dynamics

Development Tools/Service Providers

Digital

Veeva, TrakCel, Genedata, IQVIA

BioCentriq, SARTORIUS, Lonza, PerkinElmer, elevatebio, Miltenyi Biotec, Sangamo THERAPEUTICS, wood.

Market: Trends

Autologous vs. allogeneic: Personalized treatments vs. scalability and Big Pharma investments

Prioritizing **clinical trials success** over revenue generation; Partnerships with gene therapies

Moving from third-line to **second-line treatments and testing for first-line** with tech developments

Candidate-centric: one main pipeline with several variations turning companies into **platforms**

Market: Leaders

Asia-Pacific region is the fastest growing market

Characteristics:

- **Startup:** Successful phase 1 and phase 2 trials
- **Startup:** Potential for scalability
- **CDMO:** disrupts production efficiency
- **Big Pharma:** Enough capital to support production

Incumbents

BAYER · GILEAD · Pfizer · Johnson & Johnson · moderna

Startups

CRISPR THERAPEUTICS · ARCELLX · AsherBio · TreeFrog · kyverna

Regulation

Why regulate?

Unobserved long-term effects

Invasive procedures

GVHD and rejection risk

Present

- **Global standardization** through cross-country cell therapy councils (ICH)
- **Allogeneic-focus:** follow-up, production, & donors
- 21st Century Cures Act: Fast Track, Breakthrough, RMAT
- 361 Products tightening regulations

Future

- **International partnership** guidelines for shipment and access to information
- Shortening review periods
- Tighter rules for **AI & robotics** CDMOs
- Price pressure for premiums

Comparing Treatments

	Cell Therapy **Live Cells**	Traditional **Synthesized Drugs**
+ PROS	• Single treatment potential • Regenerative quality	• Predictable pharmacology • Off-patent generics • Established regulations
— CONS	• High costs for manufacturing • CRS, GVHD, & rejection • Preliminary	• Diminishing efficacy • Multiple treatment rounds

Stem Cells: Overview

Source

- Blood
- Umbilical Order
- Bone Marrow
- Fat Tissue

Use Cases

- Organ Regeneration
- Brain Disease
- Blood Disease
- Heart Disease

Collection

Autologous

+ Personalization and lower rejection risk
– Higher costs and variable regeneration

Allogeneic

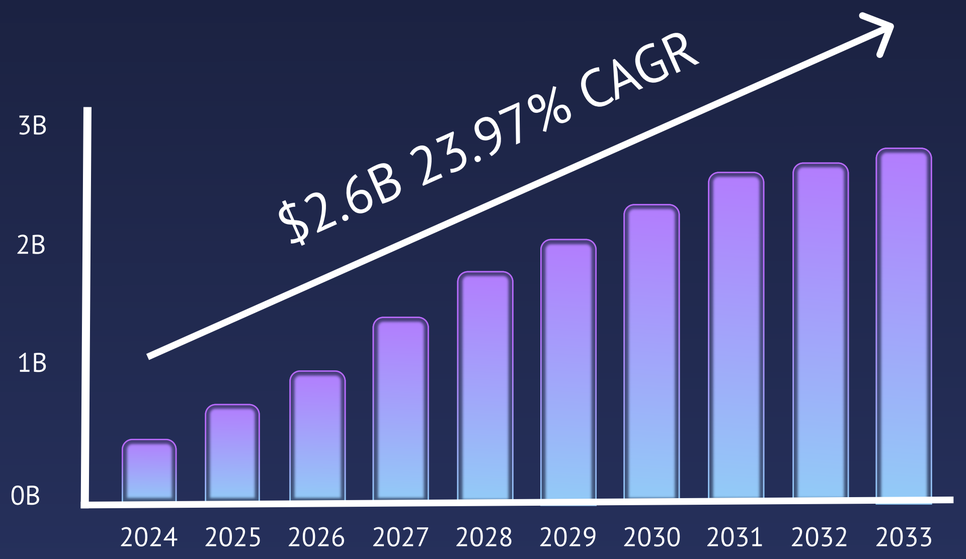
+ Immediate availability & younger cells
– Donor match; needs immunosuppression

Develops into new cells

Regenerates to replace cells

Replicates many times over time

Stem Cells: Market



Types

ESC	ASC	MSC	iPSC	HSC	EV
Embryonic Stem Cells	Adult Stem Cells	Mesenchymal Stem Cells	Induced Pluripotent Stem Cells	Hematopoietic Stem Cells	Stem cell-derived Exosomes

Value Proposition:

- Regenerative qualities
- Alterations to core tech for new pipelines
- Personalized treatments
- Treatment of incurable diseases

Mature

AstraZeneca

VERICEL

BLUEROCK

Startups

OSSIUM HEALTH

cellino

MORPHOCELL

Growing Regions

United States

Japan

Europe

Stem Cells: Trends

- Tightening Regulations
- Robust Clinical Rational
- Clear Differentiation

TREND	iPSC Growth	MSC Dominance & Exosomes Focus	Gene Editing & Synthetic Biology	Hard-to-Treat Clinical Validation	Stem Cell-Derived Exosomes
VALUE	**Risk Diversification**	**Established Regulatory Paths & Market Saturation**	**High-Value Exits + IP Moat**	**High Potential for Underserved Areas**	**Reduced Immunogenicity & High Scalability**
LIMIT	High Scale-up Costs	Difficult Quality Control	Regulation & Germline Modification	Extensive Clinical Risk	Early-Stage Space & Mechanistic Uncertainty

Stem Cells: Investments

M&A

Typically done by **Big Pharma** for a pipeline of multiple therapies and to fill knowledge gaps

- **Bayer & BlueRock** (2019) $1B, iPSC platform
- **Vertex & Semma** (2019) $950M, stem cell-derived insulin-producing beta cell

Valuation Drivers

- Broad stem cell platform → higher pre-money
- Accelerated regulatory pathways
- High chance for phase II/III success

Top Stem Cell Types

MSC

More funding towards GVHD or Crohn's, but not cardiovascular or neuro due to oversaturation. Must raise $10-$50M for viable treatments

iPSC

Newer treatment but large funding rounds from $50-$200M shows platform appeal and treatment of rare diseases

HSC

Novelty is the biggest differentiator because traditional bone marrow transplants are well-established

EV

Fewer companies w/ most at preclinical. Exosomes are the next frontier: low immunogenicity & no tumorigenicity

Stem Cells: Thesis

Highly-specialized with differentiated stem cell candidates for more **effective** & **trustable** treatments

Allogeneic source for scalability with strong **CDMO** partnerships and successful clinical trials

Neurological disorders, type 1 diabetes, & Cardiovascular Repair; **inconsistent success rates**

Identifying **first mover** robust moats in emerging sectors like stem cell-derived **exosomes**

CAR-T: Overview

Indications

- Hematologic malignancies like B-cell acute lymphoblastic leukemia, non-Hodgkin lymphoma, and multiple myeloma

Emerging Areas

- Trials are exploring solid tumors (e.g., glioblastoma, sarcoma) to expand therapeutic impact

Engineered T cells **target** specific cancer antigens

Long-term remission via **immune memory**

Source

Patient's T Cells

Donor T Cells

Use Cases

Blood Cancers

Solid Tumors

CAR-T: Market

Breakthrough **clinical efficacy, expanded treatment indications, and legislation** are key drivers propelling the CAR-T market.

Value Proposition:

- Precisely engineered T cells attack cancer cells
- Achieves durable, lasting responses
- Personalized treatments

Mature

NOVARTIS

Kite Pharma

Bristol Myers Squibb™

Startups

TMUNITY

Celyad Oncology

Autolus

Growing Regions

North America

Asia

Europe

CAR-T: Types & Limits

Types

ABECMA

Approved for adult patients with r**elapsed/refractory multiple myeloma** who have undergone **at least four prior therapies.**

BREYANZI

Indicated for adult patients with **relapsed/refractory large B-cell** lymphoma **after two or more** systemic therapies.

TECARTUS

For patients with relapsed/ refractory mantle cell lymphoma and for adults with relapsed/refractory B-cell precursor ALL.

CARVYKTI

Approved for patients with relapsed/refractory multiple myeloma following **four prior lines of therapy.**

KYMIRAH

For adults with relapsed/ refractory DLBCL and for patients **up to age 25** with relapsed/refractory ALL.

YESCARTA

Approved for patients with relapsed/refractory DLBCL, primary mediastinal B-cell, high-grade B-cell, and follicular lymphoma after **two or more lines of systemic therapy.**

Limits

CAR-T therapies are **limited by complex, costly** manufacturing processes and safety risks like **cytokine release syndrome and neurotoxicity.** Additionally, issues such as **antigen escape,** poor efficacy in solid tumors, and **suboptimal T cell persistence** further challenge their long-term effectiveness.

CAR-T: Investments

The global CAR-T cell therapy market has seen substantial investment, with reports indicating over **$141.2 billion** raised through venture capital, IPOs, licensing deals, collaborations, and M&A transactions.

M&A

Done by **Big Pharma** for a pipeline of therapies

- **Celgene & Juno** (2018) $9B
- **Gilead & Kite** (2017) $11.9B

Valuation Drivers

- Clinical Success & Curative Potential
- Platform and pipeline potential
- Manufacturing Scalability

CAR-T: Thesis

Engineered T cells show curative potential for hematologic malignancies

Off-the-shelf solutions promise **reduced costs** and **faster turnaround times**

Efforts to expand into solid cancers face obstacles like **antigen escape** and **tumors**

Natural Killers

Overview

Naturally-produced white blood cells

Identifies & eliminates “ sick” cells w/o prior sensitization

Types

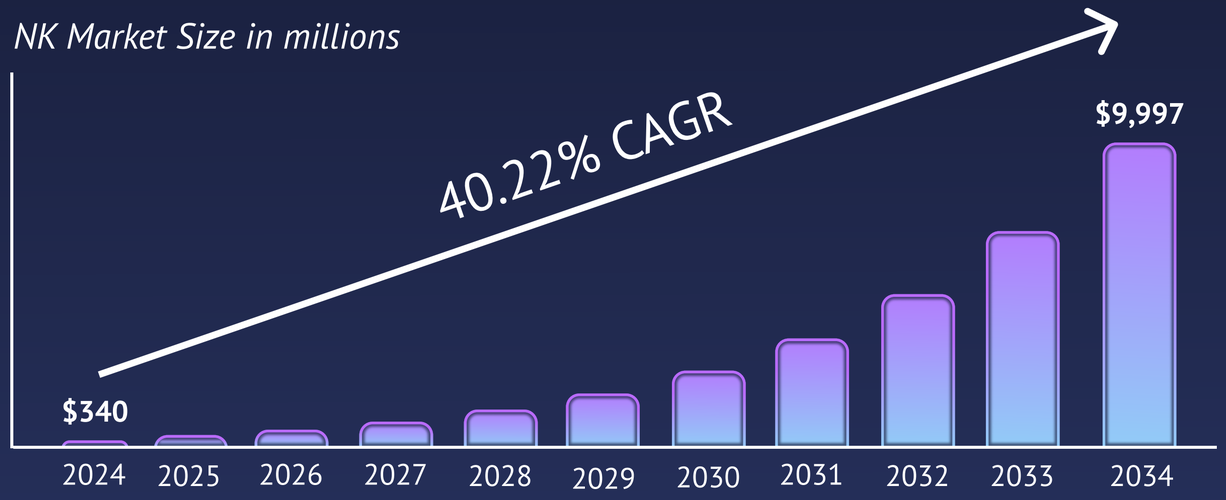
Autologous NK Therapy

Allogeneic NK Therapy

iPSC
Induced Pluripotent Stem Cells

CAR
Chimeric Antigen Receptors

Natural Killers: Market



Testing

165 Phase 1 NK Trials

92 Phase 2 NK Trials

3 Phase 3 NK Trials

Regulation

By 2024, 3 NK Treatments were approved by FDA for **Fast Track Designation**

Mature Companies

nkarta

artiva

GILEAD

Startups

Dragonfly THERAPEUTICS

SHORELINE biosciences

INDAPTA THERAPEUTICS

Natural Killers: Value Prop

Safety

NKs do not cause GVHD and limits Cytokine Release Syndrome

Acts as safety measures for Allogeneic therapies

Lifespan

NKs have shorter lifespans and naturally clear in ~2 weeks

Eliminates potential long-term side effects

? Simple

NKs are generally less complex than other cell therapies like T cells

Improves large-scale batch consistency

Compatible

NKs don’t require Human Leukocyte Antigens (HLAs) matching

Expands applicability to all patients

Natural Killers: Limits

Limited Lifespan

Administered cells naturally clears in ~2 weeks

Repeat Dosing

Patients need multiple dosing cycles for allogeneic NKs

Implications

Insurance Friction

Chronic care with a cell therapy price tag

FDA Uncertainty

Tighter regulations on dosing schedules

Natural Killers: Thesis

Notable Activity

Nkarta Therapeutics

$250M IPO *June, 2020*

Artiva Biotherapeutics

$167M IPO *July, 2024*

AstraZeneca & EsoBiotec

$1B M&A *March, 2025*

NKs make Allogeneic treatments **safer** and more **compatible** for scaling to **mass production**

NKs have an **unforeseeable future** with no FDA-approved treatments and lack of insurance policies

Industry Activity

Top Advancements

Allogene Granted 3 FTDs

Allogeneic CAR-T Cell Therapies
Phase 1 & 2 Trials *Apr, 2025*

Roche Acquires Poseida for $1.5B

Allogeneic CAR-T Cell Therapy
Phase 1/2 Trials *Nov, 2024*

Pfizer Invests 8% in Caribou Bio

4 Allogeneic CAR-T Cell Therapies
Phase 1/2 Trials *Nov, 2024*

Implications

- Big Pharma is willing to pay for secure Allogeneic
- Regulatory Validation is catching up with pipeline development

Exit Opportunities

M&A

Highly Likely by Big Pharma as they have the expertise and capital for mass manufacturing Allogeneic Therapies from startups

Pfizer AstraZeneca J&J

IPO

Less likely to happen as startups don't have enough capital to complete trials but tech advancements could reduce complications

Fate THERAPEUTICS artiva nkarta

Investment Thesis

Invest in Proven Allogeneic Startups*

Scalable & Cost-Efficient Model

Off-the-shelf production cuts costs by up to **70%**, enabling **broader access** and faster revenue scaling

Faster Delivery, Lower Risk

Short turnaround times reduce patient drop-off and capital burn, addressing key **capital** and **liability** concerns

De-Risked Targets Drive M&A

Focus on **Phase 1/2 allogeneic** startups as Big Pharma seeks de-risked, scalable assets

Appendix

Industry Calls

Victor Shapiro

- https://www.linkedin.com/in/victorshapiro/

Mark Bamforth

- https://www.linkedin.com/in/mark-bamforth-b1001410/

- https://www.mordorintelligence.com/industry-reports/cell-therapy-market
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