BioForward

The 'Roadmap for Growth' Life Sciences Event

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Workshop four:

Accelerating Patient Access to Cell and Gene Therapies via Integrated CRO, CDMO and Sponsor Partnership

Jennifer Pietrowski
Thermo Fisher Scientific

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Accelerating Patient Access to Cell and Gene Therapies through integrated CRO, CDMO and Sponsor partnership

Jennifer Pietrowski
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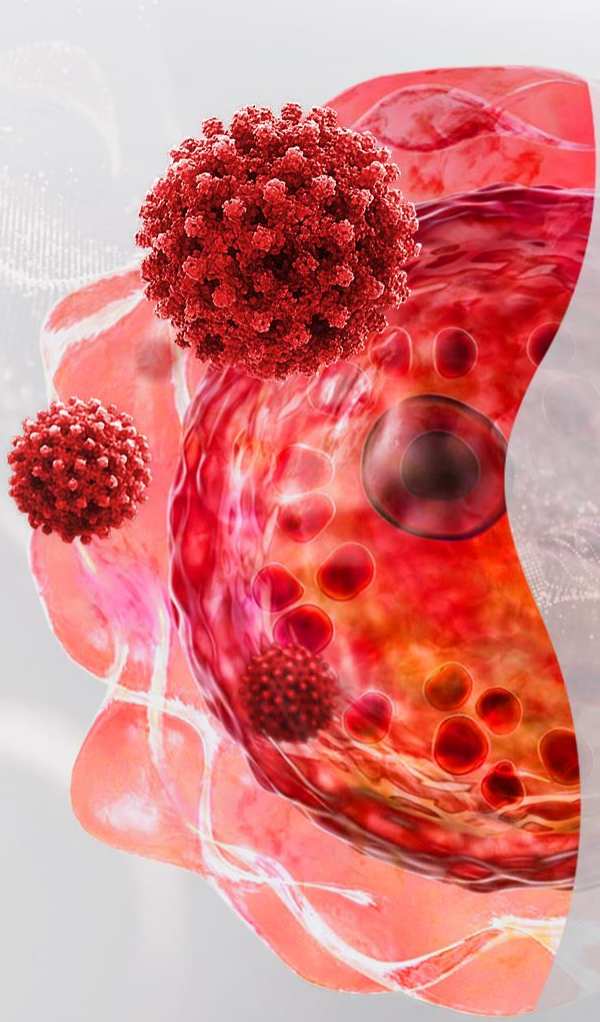
26 September 2023



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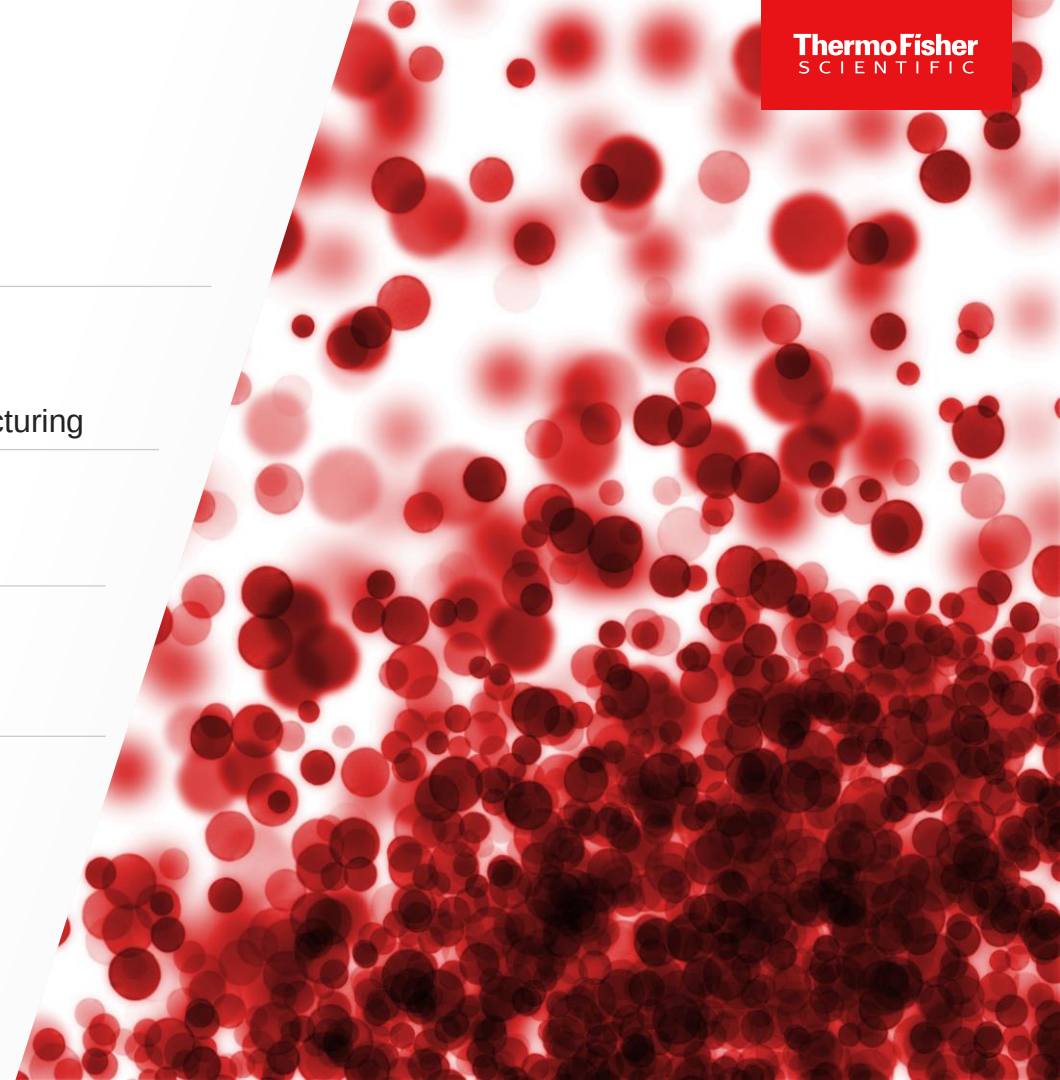
Agenda

1. Cell and Gene Therapy Potential
2. Complexities of Cell and Gene Therapy Manufacturing
3. Complexities of Cell and Gene Therapy Clinical Development
4. How Thermo Fisher Scientific can help you



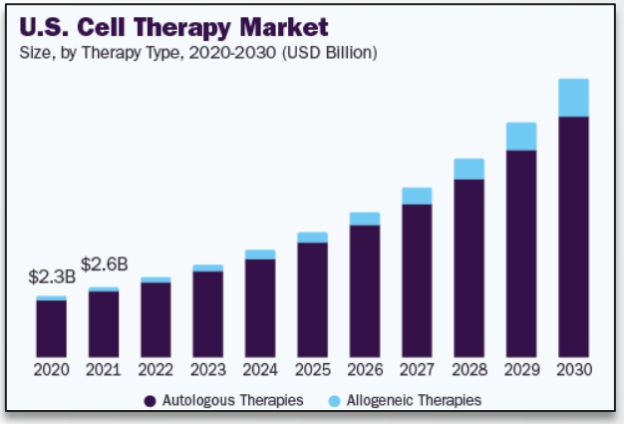
An evolving market landscape

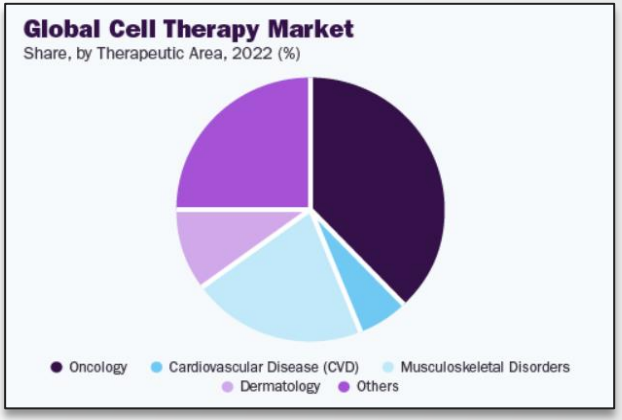
Growing market[1]

- Global cell therapy market valued at $4.77B in 2022
- Projected to grow at a compound annual growth rate (CAGR) of 16.5% from 2023 to 2030
- Oncology and rare diseases most targeted groups

Possible regulatory decisions in 2023 – Cell therapies[2]

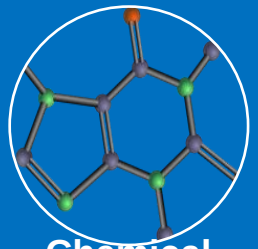
- Afami-Cel – Advanced synovial sarcoma (Adaptimmune Therapeutics)
- HPC Cord blood – Unrelated donor hematopoietic progenitor cell transplantation (StemCyte)
- Lifileucel – Metastatic melanoma (Iovance)
- Omidubicel – Hematological malignancies (Gamida Cell)
- Remestemcel-L – Steroid-refractory acute graft vs. host disease (Mesoblast)
- Tab-cel – Epstein-barr virus associated post transplant lymphoproliferative disorder (Atara Biotherapeutics)





1. Grand View Research. Cell therapy market size, share, & trends analysis report by therapy type, by therapeutic area, by region, and segment forecasts, 2023-2030.
2. Alliance for Regenerative Medicine Sector Snapshot, April 2023.

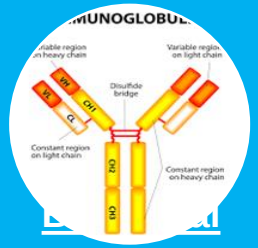
Classification of Medicinal Products



Chemical

often a small molecule obtained by chemical processes

e.g. Atorvastine



an organic molecule, manufactured in a living system such as a cell

e.g. Monoclonal antibody (mAb), miRNA

Advanced Therapies Medicinal Product (ATMP)

Somatic cell therapy

Gene therapy

Tissue Engineered

➢Adoptive cell therapies are complex biologicals that are based on tissues or cells.

➢Unlike chemical or other biological medicines, cell therapies are derived from human donor cells which are then manipulated to become the medicine.

➢As a result of being human cell derived, complexities associated with investigating these therapies are different from other trials.

What Are the Key CGT Types and How Do They Differ?

Gene Therapies

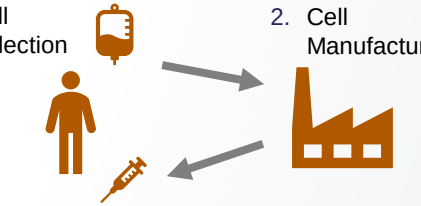
1. Centrally manufactured product

2. Patient receives 1-2 injections
3. 5-15 year (typically) annual patient follow-up

Cell Therapies

~50% allogeneic | ~50% autologous

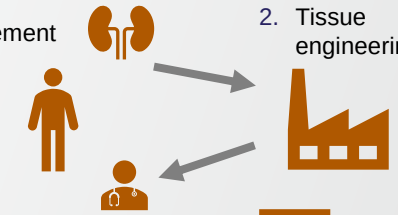
1. Cell collection
2. Cell Manufacturing



3. Injection
4. Follow-up

Tissue Engineering

1. Tissue procurement
2. Tissue engineering

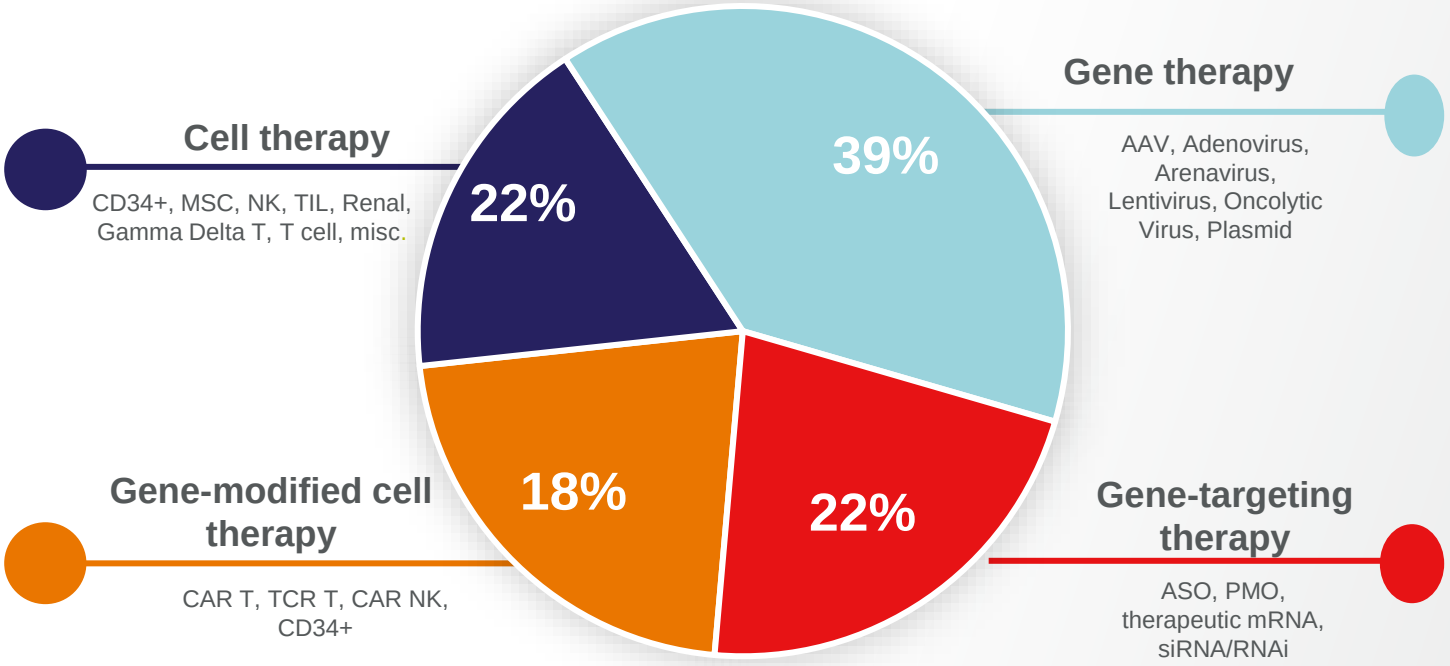


3. Surgery / transplant
4. Follow-up

Lowest complexity → *Highest complexity*

Cell and Gene Therapy by modality

Five years – 135+ studies supported



Primary Indications
Anemia, Sickle Cell
Arthritis
Cancer, Breast
Cancer, Head and Neck
Carcinoma, NSCL
Cystinosis
Diabetic Foot
Diabetic Peripheral Neuropathy
Gaucher Disease
Immunologic Deficiency
Kidney Diseases
Leukemia
Lymphoma
Leukodystrophy
Melanoma
Multiple Myeloma
Periventricular Leukomalacia
Pompe Disease
Scleroderma
Solid Tumors (other)
Wiskott-Aldrich Syndrome

Our offerings fit into an end-to-end solution for clinical trial development

PPD has supported **>130** clinical trial studies in **5** years

Customer journey

- Discovery and research
- Product and process development
- Clinical trials
- GMP manufacture

PPD now part of Thermo Fisher Scientific

Media, supplements	Process development	CMC documentation	**Regulatory support**	**Sponsorship**	Clinical scale manufacturing Plasmids
Reagents	Process scale-up	Logistics support	**Analytical services**	**Clinical protocol**	
Beads, antibodies	Analytical assay dev	Distribution		**Site selection**	Clinical scale manufacturing Viral vectors (VVs)
Analytical instruments	In-process, ret' testing	Correlative analysis		**IRB approvals[1]**	
Assay kits	Plasmid development	Database hosting		**Safety and reporting**	Clinical scale manufacturing Cell therapies (CTx)
Target ID and validation	Viral vector development			**CTA/CRF creation**	
Digital, automation, AI	Cell therapy development			**Biostatistics**	Commercial scale manufacturing plasmids, VVs, and CTx
Closed and automated Manufacturing platforms				**DSMB[2]**	
Vectors and plasmids				**Monitoring, auditing**	Clinical & commercial scale manufacturing for mRNA
				LTFU[3]	

Includes customizable lab services that apply CT-specific methodologies and instrumentation

Supporting business model

- Products
- CDMO
- CRO

Our offerings

1. Institutional Review Board
2. Data and Safety Monitoring Board
3. Long term follow up

Offerings seek to build on patient-centered research and improve patient experience by incorporating the patient voice into clinical trial design, providing early education, and leveraging key learnings

Considerations – Starting with the End in Mind

Supply Chain

- Raw material grade
- Inventory availability

Formulation and Packaging

- Target tissue
- Route of administration
- Package composition
- Storage conditions

Manufacturing Infrastructure

- Build
- Buy
- Outsourced
  - Early phases
  - Through commercial

Patient and Market Access

- Regulatory Challenges
- HTA/Payer Considerations
- Patient Pathways

Logistics

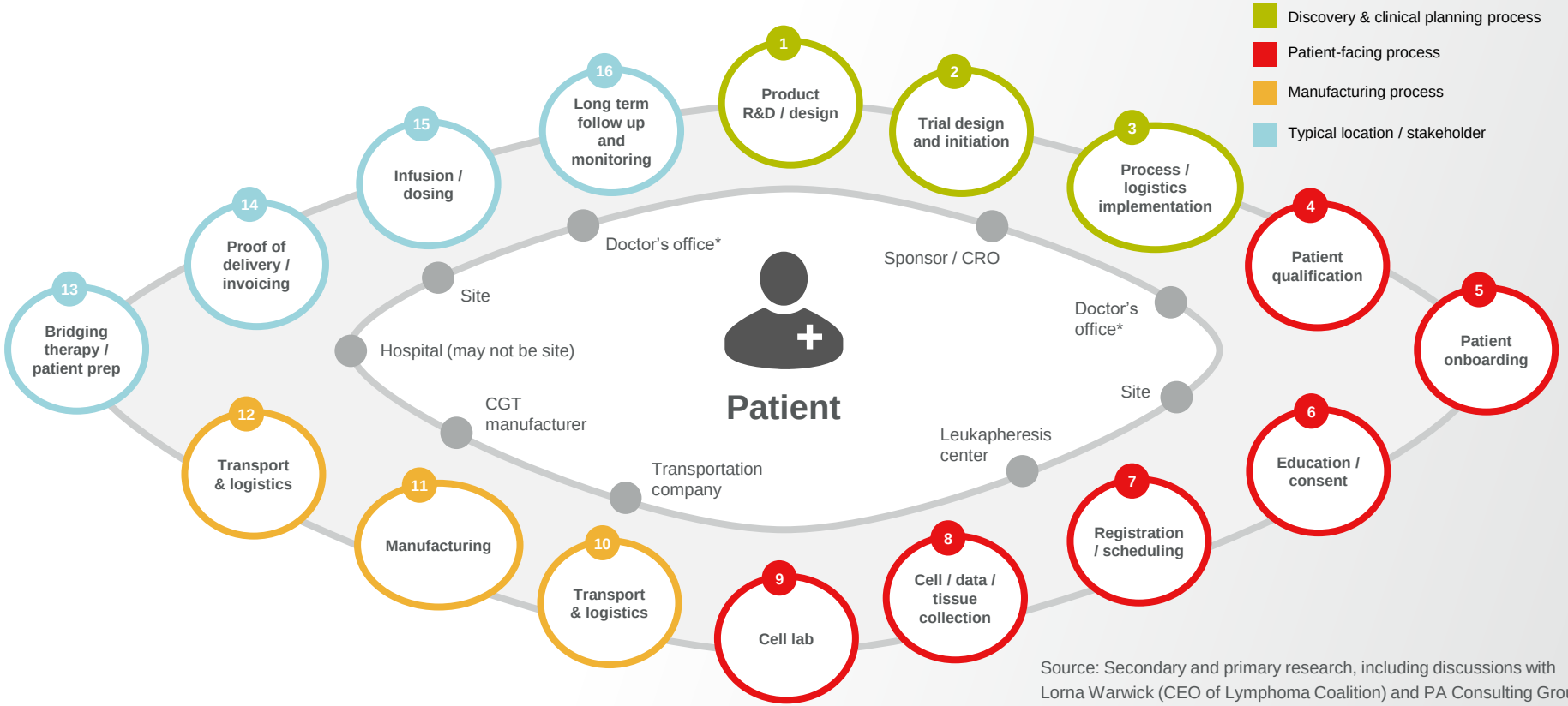
- Domestic vs International
- Geographic Considerations
- Import/Export Restrictions

Other Considerations

- IBC Approvals
- Site Accreditations
- Intellectual Property

The CGT clinical value journey is complex

Long and nonlinear patient journey involving several stakeholders and locations



Source: Secondary and primary research, including discussions with Lorna Warwick (CEO of Lymphoma Coalition) and PA Consulting Group

* Could be different doctor's offices for Steps 4 and 16

Improving Patient Journey for CGT Trials

Recruitment

+ CGT trials are complex, SOC is taxing for patient

Education & Informed Consent

+ Awareness and willingness to enroll requires empathy in information sharing

Patient Logistics & Travel

+ Complex supply chains & patient logistics

Complex care needs

+ Patients require complex care before, during, and after therapy

Follow-up requirements

+ Up to 15-year long term follow-up monitoring is required

Solution

Incorporate Patient Voice into trial design

Early education to raise awareness

Collaboration across CGT value chain

Patient and Site Services

Digitization & Decentralized Trials

>10 years of CGT clinical research experience

Delivering sponsor's assets through clinical development and beyond

CLINICAL RESEARCH

Clinical research benefits

- Tapping into medical scientific expertise across the industry through PPD's CGT Institute and I-O and Cell Therapy Center of Excellence
- Real time and continued operational best practices through Operational Centers of Excellence and Training Academies
- Collaboration and control through established governance and operational model with focus on talent
- Access to patients through established relationships with CGT Investigator Sites globally
- Services and intelligence specific to CGT in regulatory, market access and established capabilities for the development of a CGT asset

Positive impact and risk reduction for sponsor

- Institute serves in an internal **strategic advisory capacity**
- Study teams have access to **SMEs** when questions arise
- Sponsors have access to this **Thought Leadership** in the CGT space

- **Continued Training and sharing** of lessons learned and experiences, best working practices and data repositories, in real-time
- Based upon global corporate experience, successful operational delivery includes:
  - **Monitoring over >1,000 Clinical sites, >4,000 Patients dosed and ~$1B clinical development investment**

- **Flexible model** allows for resources to be mobilized to ensure data integrity and currency
- Proven ability to recruit and retain top talent with CGT experience over the past 20 years; 15% growth YoY over the last 5-years
- CGT CRAs >20% of total global resource pool, with >20% of professionals >3-years of real-world experience

- Our **experience with Sites** will enable a more personal, faster start-up, and efficient continued study management
- Enhanced enrollment planning based upon real world site metrics

- Deep **Regulatory** intelligence in >45 countries can be leveraged across global CGT experience
- Building relationship *re* **value/payer/access** projects
- Leveraging our Industry-renowned **Digital capabilities** and **decentralized** trial solutions for LTFU studies

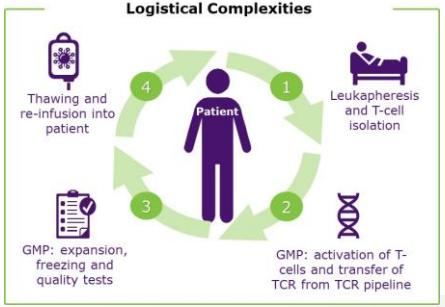
Case Study: Seamless delivery of complex Phase 2 basket ACT trial through careful logistical planning

Situation

- Ph. II autologous cell therapy protocol implemented across NA & EMEA (DEU, ESP, GRE, GRE, UK, CAN, USA): 43 sites
- Basket Trial design seven cohorts (solid tumors)
- Training stake holders across multiple departments on processes ensuring the *Chain of Custody (CoC) & Identify (CoI)*
- Negotiation of manufacturing slots
- Mitigation against short fall in procurement supplies & co-therapy supplies due to human error or supply/demand issues
- Ensuring high data currency & data quality during rapid enrollment data acquisition:
  - **Screened = 255**
  - **Procured – 183**
  - **Treated = 130**

Solution

- Establishment of executive oversight
- Logistics plan" detailing the "hand-to-hand" transfer of cellular product, including verification of "CoC"
- Communication platform
- Customized projection tool for supply chain management
- Customized projection tool for monitoring time & resource requirements (primary & floater CRAs)

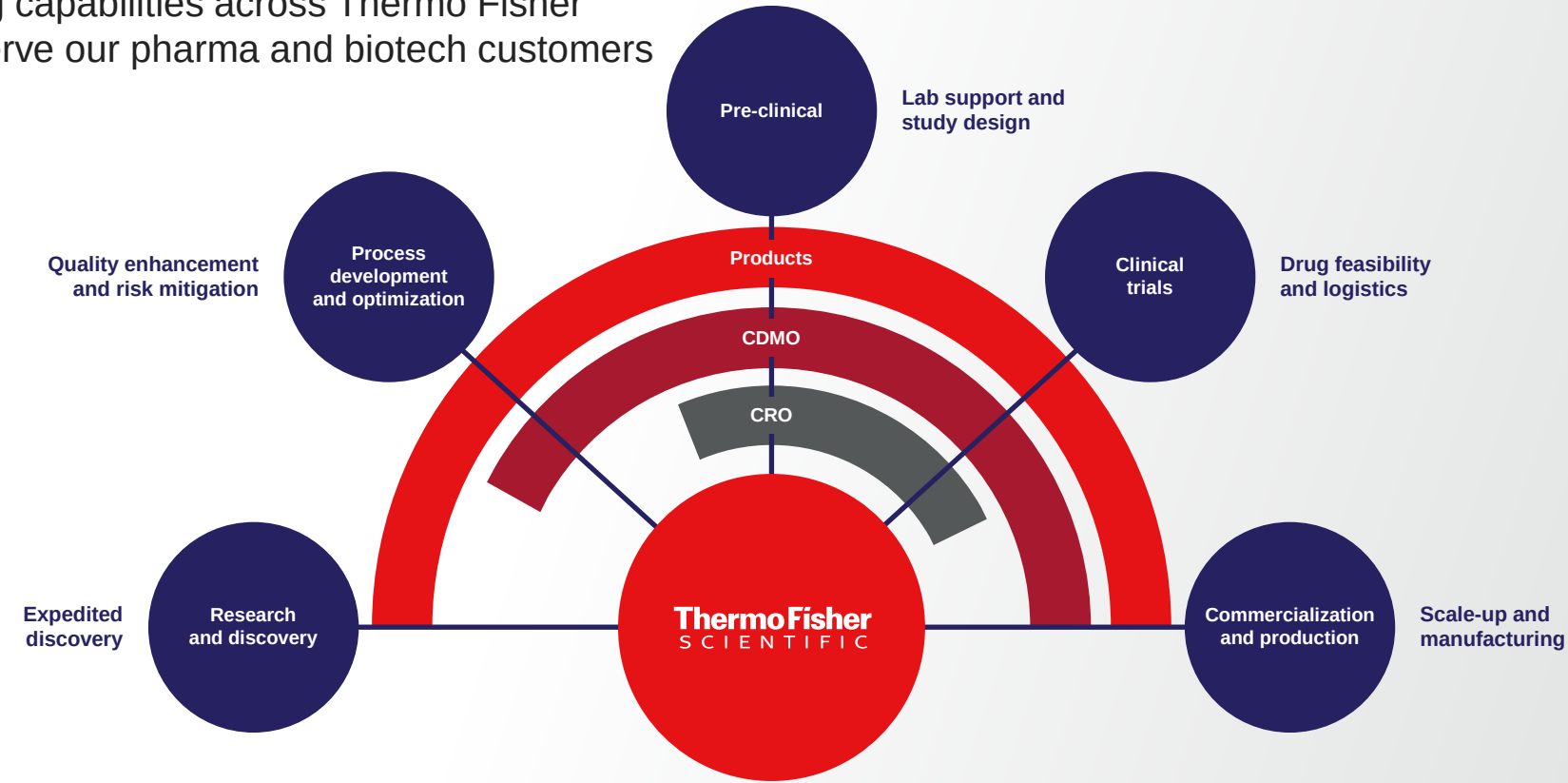


Impact

- Alignment on goals & solutions; high level customer satisfaction & subsequent non-compete award of a second study
- 183 subjects (cellular starting material procured) & 130 infusions (enrollment ongoing) completed successfully
- Global clinical logistics team interaction with sites, medical monitors, vendors accommodated schedule changes of critical events and/or supply challenges resulting from last minute short fall (supply/demand issues, temperature excursions, expiries) eliminating potential negative impacts, therefore reducing burden on site staff, sponsor, and reducing waste & cost
- Data entry, SDV and query resolution at >95%, >90%, >95%, respectively.

Thermo Fisher Scientific expanded clinical capabilities across the drug development spectrum – CDMO + CRO

Connecting capabilities across Thermo Fisher
to better serve our pharma and biotech customers



Key takeaways from understanding the cell therapy trial patient journey

CDMOs can improve patient centricity by:

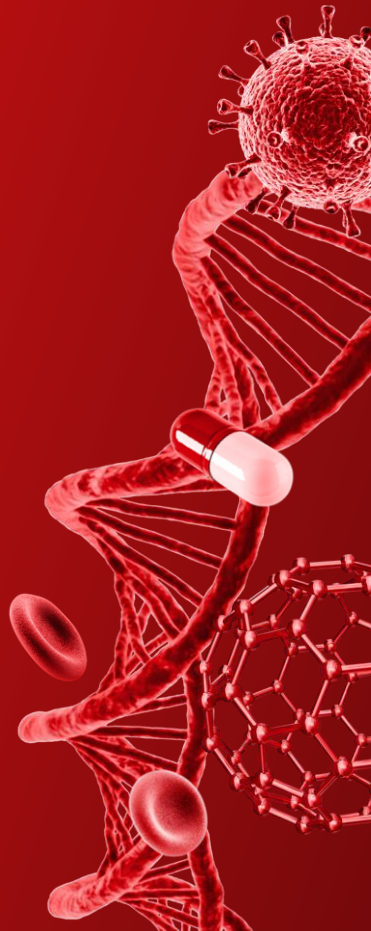
- **automating** manual processes to reduce production timelines and ultimately vein-to-vein time for patients
- **optimizing** safety and efficacy of final product through improved analytics
- leveraging robust quality systems to **mitigate risks** and **reduce time and cost**
- navigating complex **regulatory landscape** to support improved treatment accessibility

CROs can improve patient-centricity by:

- incorporating **'patient voice'** into trial design and execution
- **educating** providers and patients to raise awareness
- providing **differentiated site and patient services** across the trial
- **decentralizing** CGT trial components where possible to reduce patient burden
- **collaborating** with stakeholders across the CGT value chain

These benefits are amplified through Thermo Fisher Scientific's integrated research, development, manufacturing and clinical trial capabilities – a positively differentiated end-to-end cell therapy offering

Thank you



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