# Positioning for Global Success: Navigating CDMO Landscape for New Modalities

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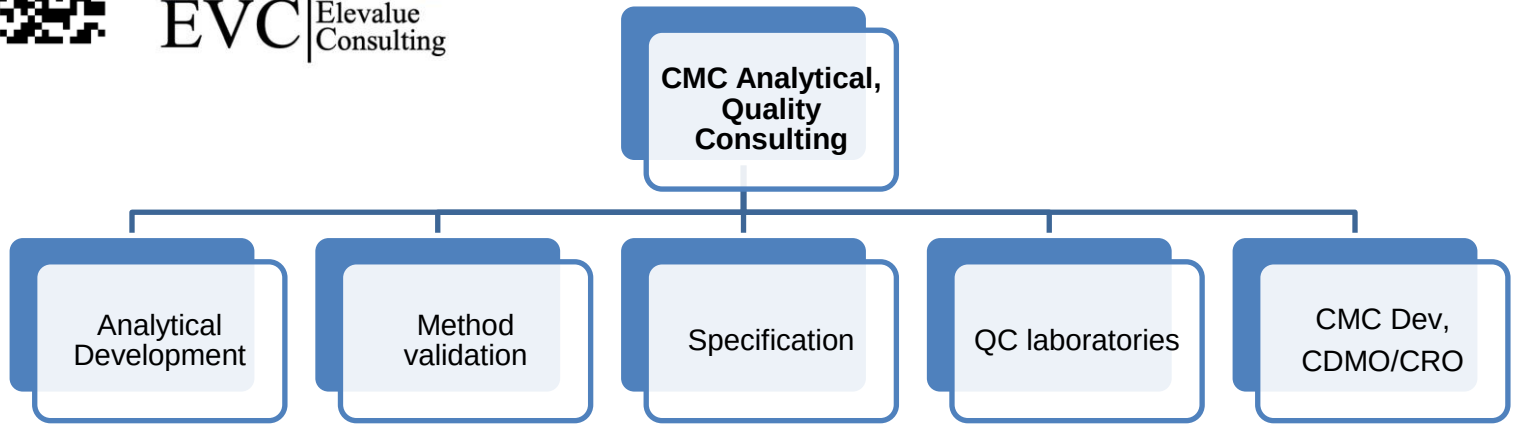
PDA Parenteral Drug Association

**PDA CDMO Partnership Workshop 2024**

CONNECTING PEOPLE SCIENCE AND REGULATION®

# CMC Analytical, Quality Consulting

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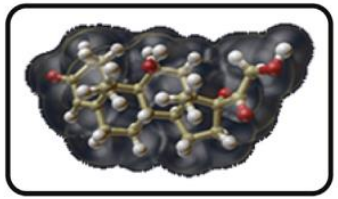
# Outline

- ❑ Introduction to Cell and Gene Therapies (CGT)
- ❑ CGT Development Overview and Challenges
- ❑ Outsourcing Needs and Considerations
- ❑ CGT CDMO Landscape and Models
- ❑ Case Studies
- ❑ Key takeaways and What's Next?

# Introduction: Cell and Gene Therapies

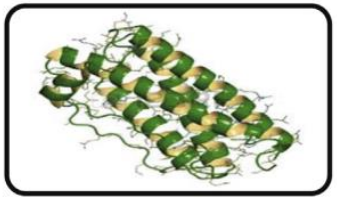
# Evolution of Therapeutic Medicinal Products

Complexity



**Small Molecules**

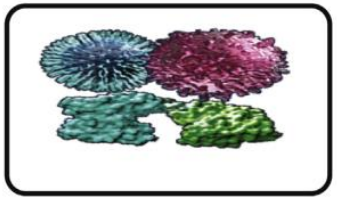
- Simple
- Single defined structure
- Predictable chemical/ reagent reaction
- Production of identical copies
- Stable
- Easy to fully characterize
- Minimal data packet



**Therapeutic Proteins**

- Large
- Complex structure
- Bank of living cells
- Identical clones unlikely
- Sensitive to environmental conditions
- Correlation of structure/ function elusive
- Robust data packet

mAb, ADC



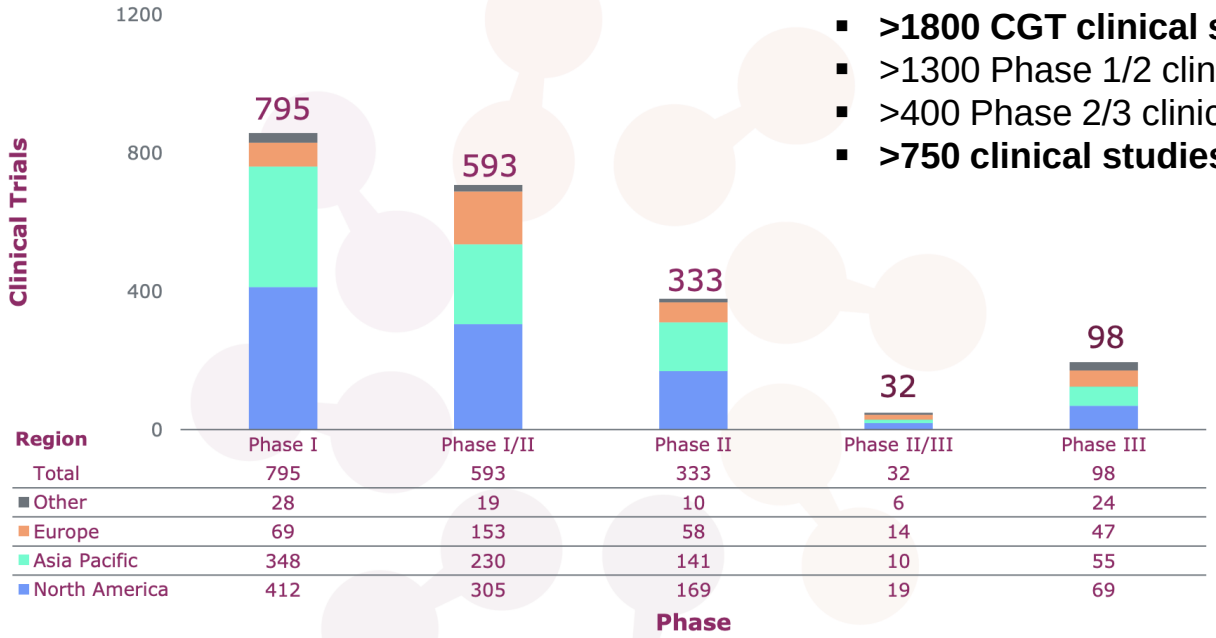
**Novel Treatment Modalities**

- Vary from small to large
- Complex and unique structure
- Varied modular manufacturing
- Heterogenous sub-populations
- Varied stability
- Personalized nature difficult and costly to characterize
- Limitless data packet

Cell and Gene Therapy

Modified from Journal of Pharmaceutical Sciences, Cauchon, N.S., et al., 2019

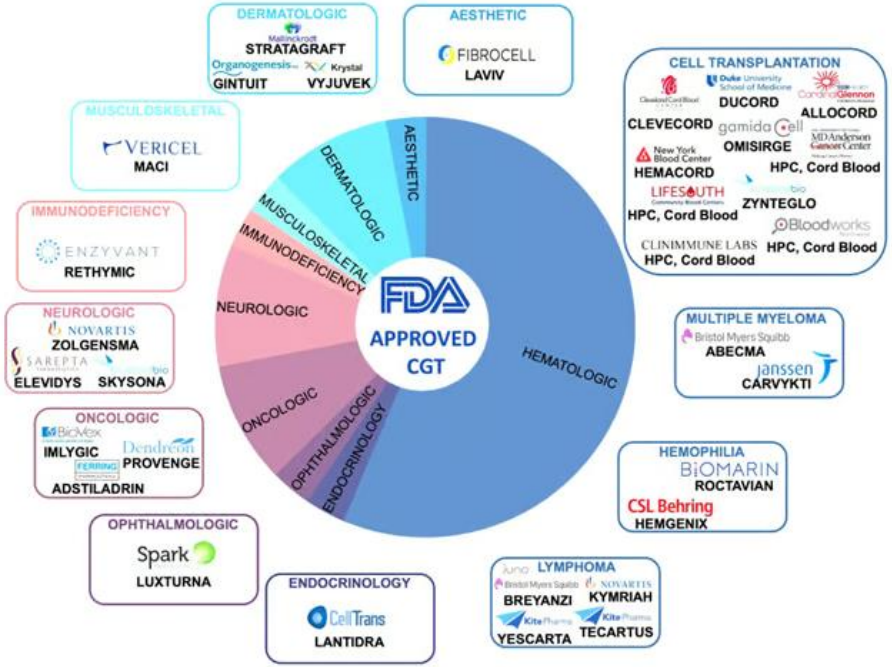
# Cell and Gene Therapies




- **>1800 CGT clinical studies**
- >1300 Phase 1/2 clinical studies – Early Stage
- >400 Phase 2/3 clinical studies – Pivotal/Late Stage
- **>750 clinical studies in Asia-Pacific**

Q2, 2024 report
Alliance for Regenerative Medicine

# FDA Approved CGT products




*32 approved CGT products by 2023 were used for the diagram

## >37 CGT products received approval in US

for various applications by the Center for Biologics Evaluation and Research (CBER)

>10 ex vivo engineered GT products in US

In 2024, FDA approved
TIL (Amtagvi) from Iovance,
TCR-T (Tecelra) from Adaptimmune

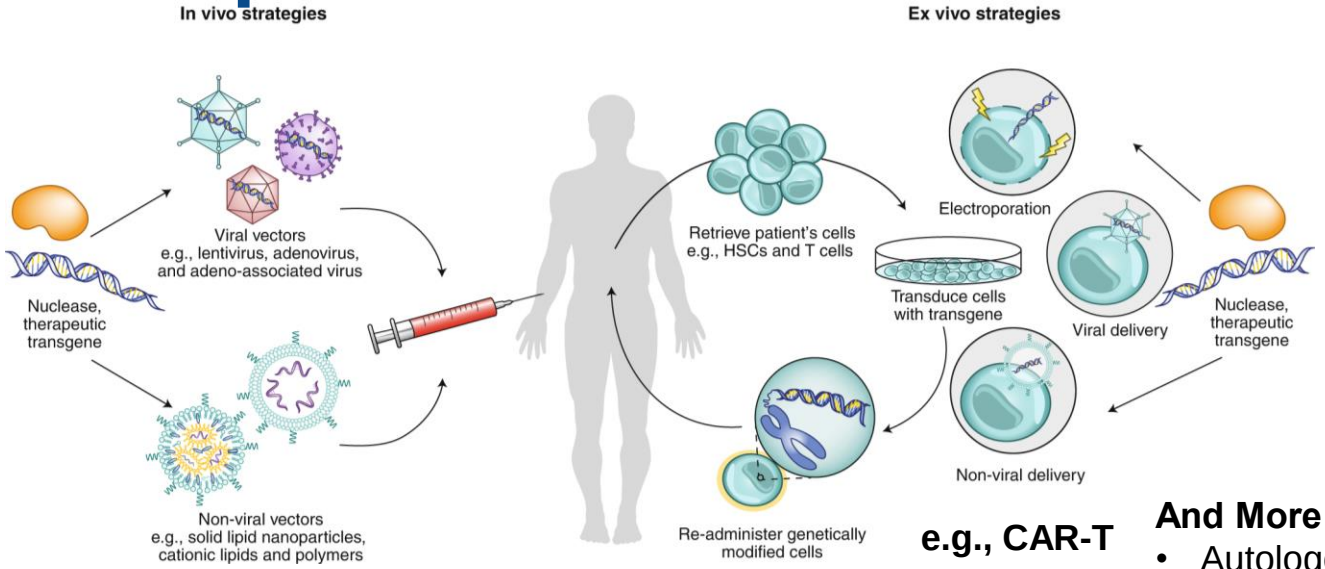
# Why Cell and Gene Therapy?

- Potential of Curing Diseases and long lasting: >10,000 Rare Diseases caused by mutation of a single gene
- Precision Medicine (personalized treatment): Personalized treatment tailored to individual's disease profile, genetic mapping
- Potential treatment options for previously untreatable diseases and difficult-to-treat diseases in hematology, oncology, ophthalmology, neurology, etc.

# Impact on Patient is Huge

- Case study of the first CAR-T patient – Emily Whitehead
- Gene Therapy for Duchenne Muscular Dystrophy


# A Snapshot of Cell and Gene Therapies




**e.g., AAV, LNP**

**e.g., CAR-T**

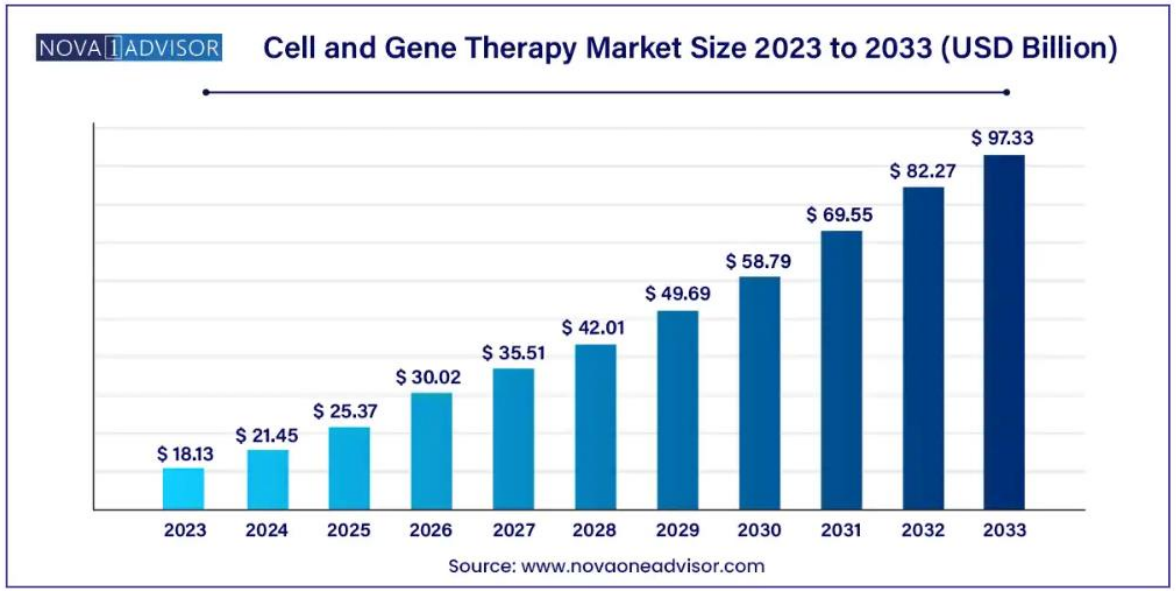
**And More…**

- Autologous vs. Allogeneic
- Regenerative medicines
- Stem cells - HSC, iPSC
- Tumor infiltrating lymphocyte (TIL)

….

Nature Biotechnology, **Haasteren, J.v. et al,** June 2020

# CGT Market Overview




- North America:  USD 8.67 billion in 2023 and it is expanding around USD 45.24 billion by 2033.
- Europe: USD 6.24 billion in 2023 and it is poised to hit around USD 30.04 billion by 2033.
- **Asia Pacific: USD 2.44 billion in 2023 and it is expected to surpass around USD 15.12 billion by 2033.**

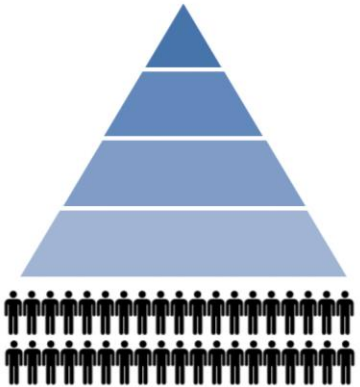
# Key Challenges in CGT Development

# Cell and Gene Therapy Development

## Paradigm Shift in Manufacturing

### Conventional Drug/Biologic

1 product lot



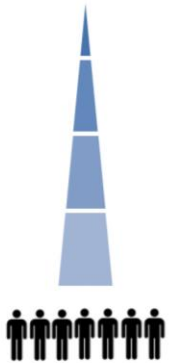
Many patients

Unique challenges

- Advanced manufacturing
- Advanced QC technologies
- Scale out
- Distributed manufacturing
- High product variability
- Comparability
- Source materials
- Distribution
- Impact of manufacturing failure

### Cell & Gene Therapy (CGT) Products

1 product lot



Few patients

1 product lot

Single patient

Dr. Steven Oh, FDA, 2024

# Challenges in Developing CGT

- ❑ New Technologies
- ❑ Complex Product & Mechanism of Action
- ❑ Risk vs. Benefit (Cost vs. Benefit) Balance
- ❑ Evolving Regulatory Landscape

# CMC Development Considerations

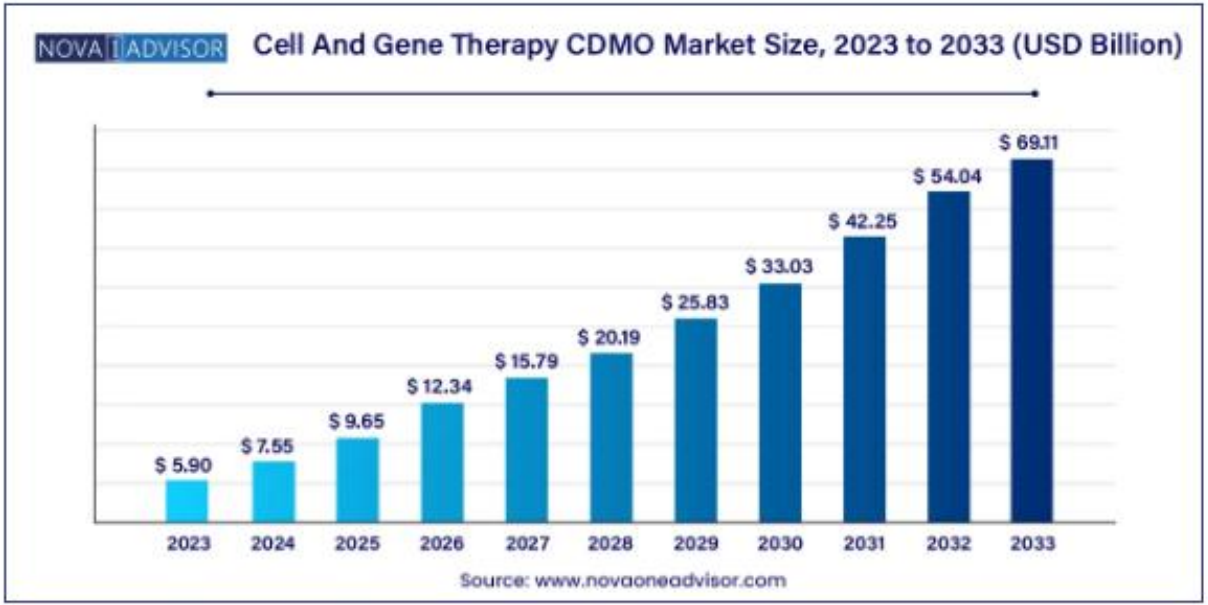
- ❑ Risk-based, Phase-appropriate approach
- ❑ Novel process technologies – e.g., Equipment for GMP manufacturing, Consistency
- ❑ Supply Chain Strategy
  - Manufacturing Strategy: Build vs. Buy, CDMO Selection, CoGs
  - Sourcing raw material, starting material – especially new reagents – GMP material available? Lead time?

# CMC Development Considerations

- ❑ Product Characterization and Control Strategy
  - Need Early Analytical Dev, New analytical technologies
  - Potency: complex MoA
  - E2E Control Strategy
  - Comparability
- ❑ Scalable cGMP Process
  - Initial IND and beyond
- ❑ Logistics of Supply Chain

# CGT Outsourcing Needs & Key Challenges

# CGT CDMO Landscape




- North America accounts for the largest share of 40.18% in 2023.
- **Asia Pacific, on the other hand, is anticipated to register a lucrative CAGR of 29.1% during the forecast period.**

# Outsourcing Needs: How to Bake a Big Pie

- ❑ Manufacturing Strategy: Build vs. Buy, or Hybrid? Know What you want.
- ❑ Large Pharma vs. Virtual start ups
- ❑ Research, Development, Manufacturing
- ❑ Sourcing Materials
- ❑ Analytical Testing

**External partnership is essential**
**for CGT Development and Commercialization**

# Key Outsourcing Challenges

- ❑ Finding the Right Partner
- ❑ Virtual Start-Up Companies with Limited CMC Expertise
- ❑ Need to Project Later Stages of Development As Applicable

## ❑Pre-Set Criteria

Examples

- Technical Expertise and Equipment
- Regulatory, Quality Compliance
- Analytical Capabilities and Tools
- Raw Materials and Scalability
- Validation and Comparability
- Capacity for scaling up/out
- Timeline
- Cost
- Culture
- Relationship management

# CGT CDMOs

❑ Different Sizes and Specialties
- Industry Giants CDMOs
- Specialty/Boutique CDMOs
- Diverse modalities
  - e.g., CART, TIL, mRNA, Virus, LNP, iPSC, in/ex vivo, ..
- Raw/Starting Materials
  – e.g., Genome editing reagents, DNA, RNA, modified oligos,.

❑ Different Regions
- North America
- Asia-Pacific
- Europe
- Geopolitical considerations

❑ Different Business Models
- Vertical integration
- Horizontal integration
- Early or late-stage programs, One-stop-shop

# CDMO Models: Pros & Cons

| Aspect | Large CDMOs | Boutique CDMOs |
|---|---|---|
| Scale | √ | X |
| Diversity | √ | X |
| Personalization | X | √ |
| Flexibility and Speed | X | √ |
| Cost | X | √ |
| Stability | √ | X |
| Regulatory experience | √ | X |
| Specialized expertise | X | √ |

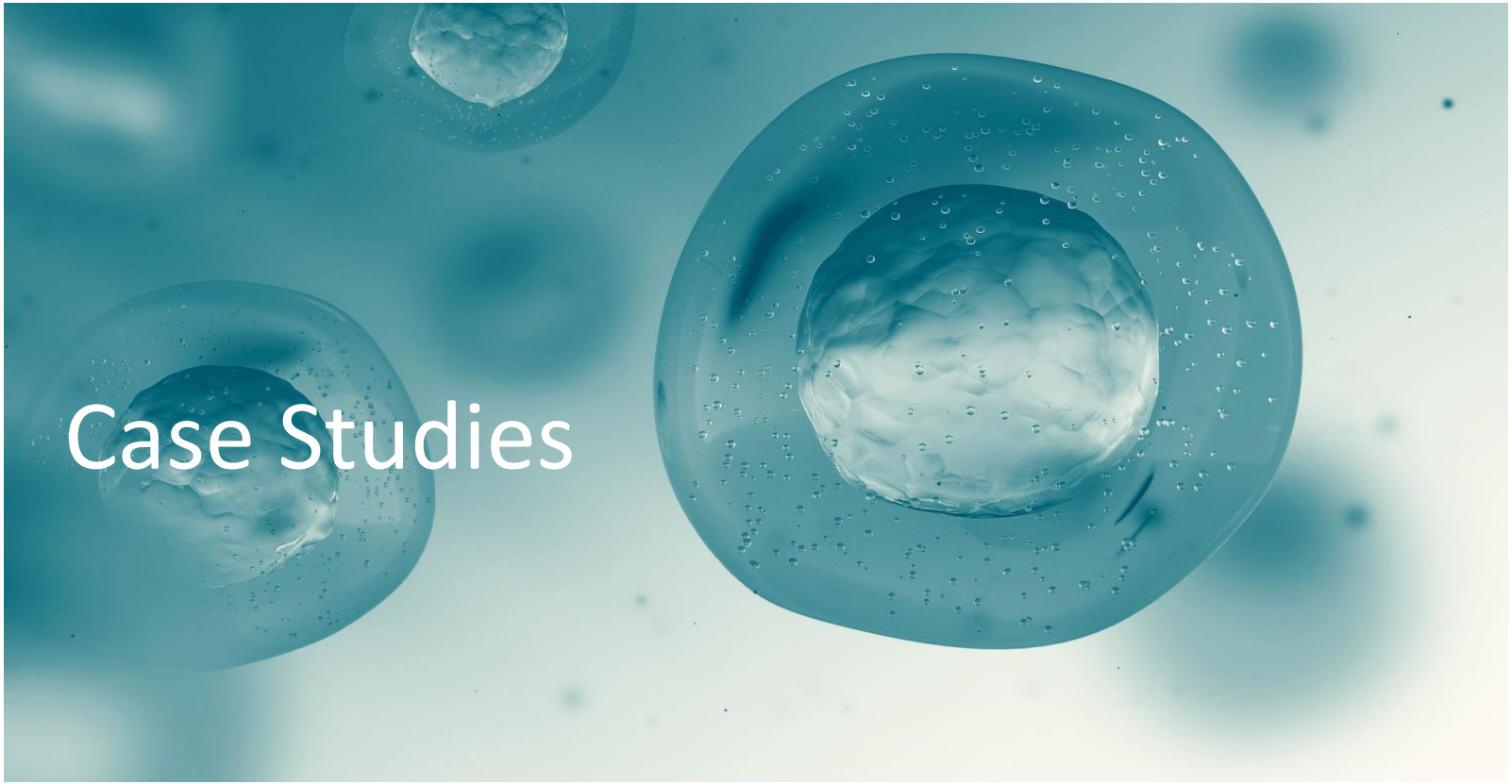
- Both large and small CDMOs have distinct advantages
- Choice depends on specific project needs:
  - Scale
  - Complexity
  - Budget
  - Desired level of personalization
- Consider a mix of both for diverse projects
- Other different CGT CDMO models exist

# CDMO Strategy for Global CGT Market

- Technical Expertise
  - Cutting-Edge Technology vs. Platform
  - Process and Analytics
  - E2E Control Strategy
- Skilled Workforce
  - Knowledge and Education
  - Experience
  - Retention
- Speed
  - Readiness for Accelerated Timeline and Approval for CGT (will be a norm)

# CDMO Strategy for Global CGT Market

- Regulatory Readiness: e.g., Audit, Inspection
- Partnerships with Innovators
- Global Presence
  - Good Communication
  - Expand for global access to markets and clients



# Case Studies – CGT Outsourcing Challenges

## Case Study 1) Critical raw/starting material:

GMP material from a qualified vendor. No quality agreement in place. Expect process and analytical changes but no obligation to update the sponsor

## Case Study 2) Different expectations in using DMF

For Early stage for IND vs. Late stage for BLA / FDA expectation

# Key Takeaways

- Speed, Expertise, Agility
- Safety and Product Quality  - No compromise
- Data integrity is a critical piece to monitor
- Cultural Fit and Communication are important part of collaboration and integration – Transparency matters
- Quality Agreement aligning expectations is critical

# Future Trends and Opportunities

- ❑ Novel MoA (hopefully with durable clinical outcomes)
- ❑ Increase Accessibility to Patients
  - Lowering CoGs and increasing Patient Accessibility
  - Implementing Automation, Platform tech
  - Industry Harmonization and Standardization as applicable
- ❑ Expand to Potential New Markets and Therapeutic Areas
- ❑ Evolution of the CDMO-Sponsor Relationship
  - Impact of Dynamic Geopolitical situation – BioSecure Act
  - Emerging technologies shaping the CDMO landscape
  - Regulatory, Business and Partnership

# Thank You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