Chasing Vector

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We urge you to consider these factors carefully in evaluating the forward-looking statements herein and you are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement. The forward-looking statements contained in this presentation speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances.

We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA.

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Adaptimmune is a leader in TCR T-cell therapy

- Scientific leadership in TCR T-cell therapy
- NY-ESO responses in two solid tumours
- MAGE-A4 & MAGE-A10 no evidence of off-target toxicity
- On track for response data 2H 2018
- Building a fully integrated cell therapy company

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Adaptimmune's Proprietary Pipeline

PROGRAM	INDICATIONS	PRE-CLINICAL	PHASE I / II	REGISTRATION
MAGE-A10	Urothelial Melanoma Head & Neck			
	NSCLC			
MAGE-A4	Urothelial Melanoma Head & Neck Ovarian NSCLC Esophageal Gastric Synovial sarcoma MRCLS			
AFP	Hepatocellular			
ADDITIONAL SPEAR T-CELL CANDIDATES				
Multiple targets/Multiple indications				

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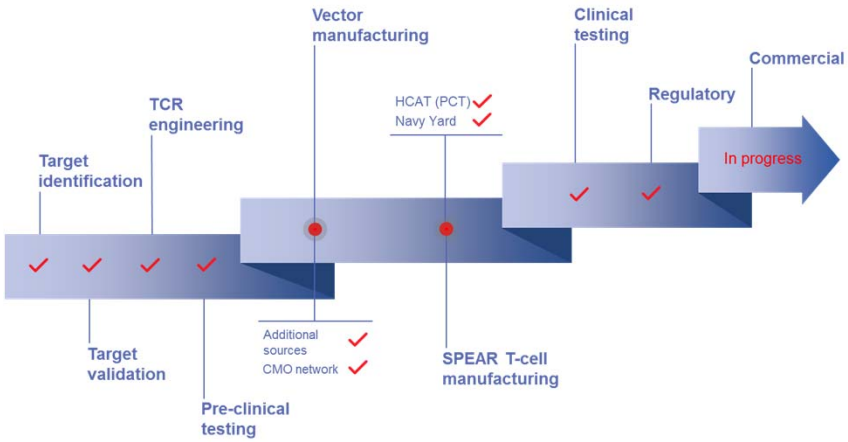
NSCLC=non-small cell lung cancer; MRCLS=myxoid/round cell liposarcoma

Becoming a fully integrated cell therapy company



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Sourcing & Procurement's MISSION

Our Mission is to identify and engage with suppliers who provide Adaptimmune with the best overall value based upon our business requirements

We do this through leading cross-functional teams in sourcing events that introduce Adaptimmune's business requirements to the marketplace

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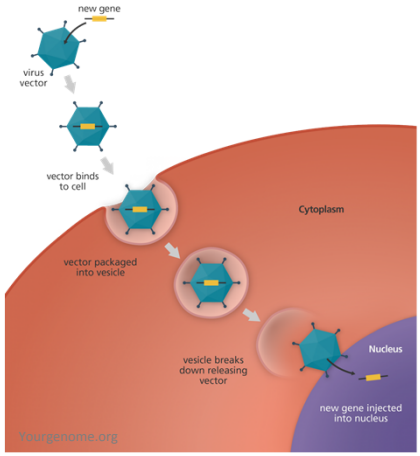
Viral Vector 101

- Viral Vectors are **essential** to the T Cell manufacturing process as they are the tools designed to deliver genetic material into cells
- In cell therapy, vector is not the drug product
- Lentivirus is a subclass of the retrovirus and is commonly used in Cell & Gene Therapy
- Modified viruses are used as viral vectors (or 'carriers'), protecting the new gene from degradation while delivering it to the "gene cassette" in target cells
- Viral vectors coerce target cells to accept and separate the new gene from the virus particle and transport it to the cell nucleus. The target cells begin using the new gene to perform its function



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Vector Market Challenges

The New York Times

Gene Therapy Hits a Peculiar Roadblock: A Virus Shortage

07 Nov 2017

Key Takeaways:

- Companies who manufacture vector are swamped with orders & requests
- Demand is outstripping capacity as new Cell & Gene Therapy companies are created
- Many companies are booking slots years in advance
- Some small biotechs have been shut out of the market entirely

Key Takeaways:

- Lead times for manufacturing slots are averaging 16 months
- Shortage of both manufacturing facilities & qualified staff
- The cost of constructing manufacturing facilities is prohibitively expensive
- The demand is most likely to drive up prices for manufacturing services

PHARMACEUTICAL TECHNOLOGY

Can the gene and cell therapy revolution scale up?

28 May 2018

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Vector Manufacturing Basics

- Critical Materials for Manufacture
  - HEK293(T) Cells frequently utilized
  - Media
  - Serum (if required)
  - Plasmids
  - Buffers
  - Consumables & packaging components

- cGMP Manufacturing Methods
  - Adherent Method
    - It is a tedious & manual process to adherently grow cells
    - Allows scale out but not scale up
  - Suspension Method
    - Uses suspension cells grown in bioreactors which increases yield and productivity
    - The downside is that this method can lead to poor efficiency and reproducibility

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Vector Complexity

- High degree of complexity with this class of biologics
  - Extensive characterization & QC testing required
  - Critical specifications must be met, such as sterility, potency and titre
  - Must have confidence in batch to batch consistency and comparability
- Quality Expectations
  - Introduction of EU ATMP GMP guideline provides some specific references to manufacturing controls of gene therapy products; this provides guidance and is gaining acceptance
  - Early phase manufacturers still have developing quality systems and may have challenges in being able to characterize their process to a level required for commercialization
  - Critical starting material requires robust lifecycle management as a complex process. Process validation and expectations for process knowledge and lifecycle documentation is required

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Inherent Risks

- Reliance on Single Use Technologies
  - Single use materials that come in contact with cell culture and vector products can impact performance, safety, quality and stability
- Biologic starting materials have significant variability
  - The potential for agent contamination carries a greater risk
  - Aseptic process requires filtering vector, which reduces titre

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All Vector is NOT Created Equal

- Quality & performance varies between suppliers
  - Wide variations in product quality & performance
    - Biological titre results determine number of doses derived per batch
      - 5 patient doses derived per 250L from Supplier A
      - 175 patient doses derived per 250L from Supplier B
      - 0 patient doses derived per 250L from Supplier C
- Significant differences in price between suppliers
  - Even when quality & performance are similar, pricing varies greatly

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Supply Chain Impacts

- Varying titre results create challenges to forecasting
  - Buying too much vector is time and resource consuming
    - Requires additional storage, planning, etc
    - The additional purchase of vector that may not be utilized further drains available capacity in the marketplace
  - Buying too little vector could be catastrophic
    - Stocking out of vector halts manufacturing and impacts patients

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Adaptimmune's Starting Point

- Academic GMP Manufacturers comprised the supply base
  - Tight capacity at each facility
  - Adherent manufacturing processes utilized
  - Adaptimmune had limited choices of supply
  - Small batch sizes due to space considerations
- Inconsistent quality & performance results between suppliers
- No quality and performance contractual guarantees
- Limited forecasting ability due to volatile nature of vector manufacturing

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The Sourcing Team's Responsibility

- Task: Secure a compliant & robust supply chain for vector
  - Execute comprehensive supply agreement(s) with world class supplier(s)
  - Obtain a continuous supply of high quality product to support manufacturing
  - Maintain focus on cost control
- Key Challenges:
  - Low volume requirements and high complexity product
  - Minimal purchasing leverage with small supply base
  - Extremely tight capacity within the marketplace
- The Solution:
  - The Sourcing Process

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Capturing Vector using the Sourcing Process

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The Sourcing Process

- Define the problem to be solved
- Set roles & responsibilities for team

- Build AQSCI requirements
- Conduct market research
- Launch RFI and cast a wide net

- Execute strategic analysis
- Generate multiple options
- Analyze Risk

- Launch RFP & finalize negotiations
- Finalize selection of supplier via AQSCI criteria

- Supplier performance management
- Evaluate potential for supply chain improvements

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Stakeholder Engagement

- Strong collaboration between Adaptimmune Teams
  - Sourcing
  - Quality
  - Manufacturing Operations
  - Process Development
  - Manufacturing, Science & Technology
- Critical cross-functional output generated
  - Clear technical & commercial AQSCI requirements
  - Critical KPI's & metrics that define successful manufacture of vector

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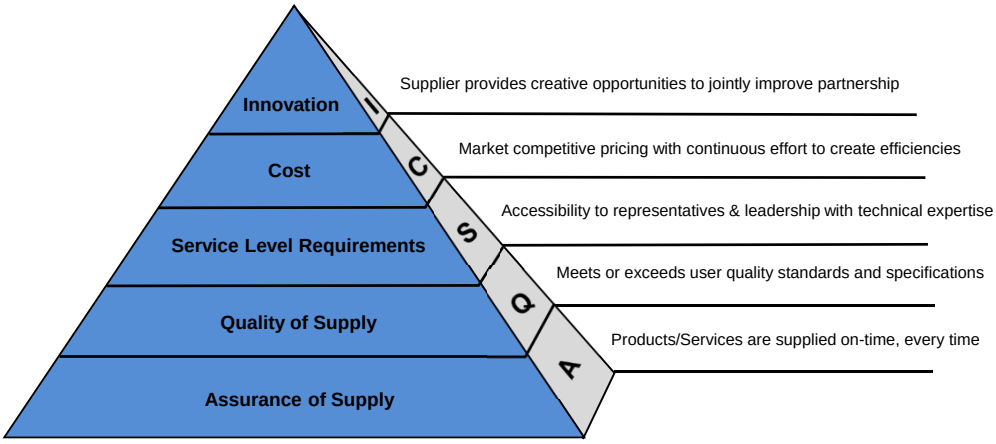
AQSCI Business Requirements



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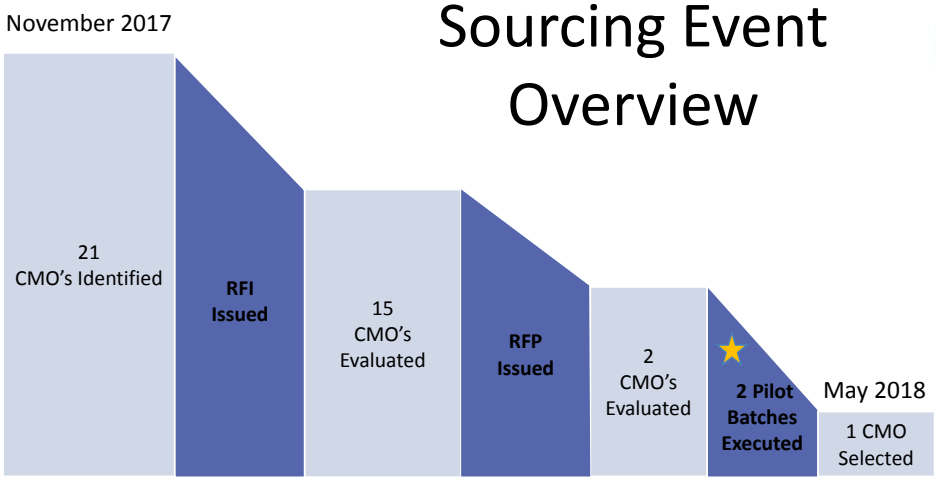
Sourcing Event Overview



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- Long-term supply deal executed
- Beneficial pricing negotiated
- Quality agreement executed
- Performance guarantees embedded
- Forecasting process established
- First batch manufactured Right First Time!

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Focus on Supplier Continuous Improvement

- Implement Governance with CMO as part of the contracting process
  - Don't wait for the first problem to arise to establish governance
- Focus on improving supplier quality & performance
  - Include improvement topics in every formal agenda
- Constant evaluation of marketplace
  - The past is a point of reference, not a place of residence
    - Who is new in the market?
    - What has changed in the past year?
    - What can be better?
    - There is no time to rest!

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Focus on Internal Capabilities

- In-house GMP Vector Development & Production
  - Agreement reached with CGT Catapult in January 2018
  - Adaptimmune will utilize its own novel vector manufacturing process for vector production
  - Ideal mix of internal and external supply that ensures risk mitigation
- About Catapult
  - Designed specifically for cell and gene therapies
  - 7000+m^2 manufacturing centre
  - 12 large (100m^2) segregated modules

Stevenage, UK Facility

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Key Learnings

- Sourcing vector is incredibly complex!
- Trust the sourcing process
- Build AQSCI requirements as a cross-functional team
- Conduct due diligence with suppliers on-site & face to face
- Evaluate each CMO's pilot batch prior to making financial commitments
- Finish strong with a comprehensive supply agreement
- Don't settle for anything less than what you need!

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That's it

Thank you for your time and attention!

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