Academic and Industry Partnerships

Technology Transfer and Scale-Up

Stewart Abbot

8th June 2017

Disclosure

- Stewart Abbot is an employee and share holder of Fate Therapeutics Inc.
- Fate Therapeutics Inc. has an ongoing collaboration with the Regents of the University of Minnesota

Academic and Industry Partnerships
Technology Transfer

Guiding principles

- Ask not what your partner can do for you, but what you can do for your partner
  - after all it's a marriage…of sorts
- Bear in mind that each partner may have different priorities
  - Publications
  - Patents
  - Trade-secrets
  - Risk-tolerance
  - Timelines
  - Funding
- Assume it the process will take longer than the initial Gantt chart
- TPPs are useful
  - Target Product Profile
  - Target Process Profile
- Put the patients first

- 3 -

Academic and Industry Partnerships
Technology Transfer

Target Product and Process Profiles

- A basic statement of expectations of product form and function
- US FDA "The TPP embodies the notion of beginning with the goal in mind"
  - https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm080593.pdf
- Selected Attributes: T Product P's
  - Product description: Brief description and/or current product name
  - Mechanism of action: The mechanism by which the product produces an effect on a living organism (Efficacy / Potency).
  - Indication for use:
  - Expected Doses
- Selected Attributes: T Process P's
  - Process "feedstock"
  - Process yields
  - Process / product identity & purity
  - Process residuals

- 4 -

Academic and Industry Partnerships
Technology Transfer

Key Considerations (Context: IND and FIH study enablement)

- Direction of Technology Transfer
  - Technology developed in academic setting transferred to commercial partner or license holder
  - R&D conducted in a commercial setting transferred to a academic partner for clinical manufacture and clinical trial
- Stage and Environment of Development
  - Stage of technology R&D prior to transfer
    - Level of process understanding
  - Expected / necessary stage of development after transfer
    - i.e. what level of process development will be required during "transfer"
  - Expected time required for process development / transfer
  - Academic R&D environment ≠ Biotech R&D Environment ≠ Pharma R&D Environment
    - Process Understanding, nature and level of documentation
- Elements to be Transferred
  - Process complexity
    - Process AND Process QC

- 5 -

Academic and Industry Partnerships
Technology Transfer

Challenges and Approaches

- Typical Challenges
  - Overestimation of process understanding and control prior to transfer
  - Technology transfer is a great way of finding out what elements of a process are variable / not sufficiently controlled
  - Potential need to conduct "process development" during transfer
  - "Language" barriers e.g. different understanding of TLAs (QBD, CTQ, TRL etc.)
  - Aggressive sponsor timelines
  - Forgetting that QC assays may have to be transferred ahead of the process
- Typical Approaches (assumes legal agreements in place)
  - Transfer and review process documentation
    1. Research, Development, Manufacturing, QC & QA
       - Mutual definition of success metrics is CRITICALLY important
    2. On-site review and performance of process at site of process establishment ("see one" or more)
    3. On-site review and performance of process at site of process establishment ("do one" or more)
       - Perform engineering runs (selected unit operations or entire process)
       - Perform Process Qualification (PQ) runs on entire process

- 6 -

Academic and Industry Partnerships
Process Scale-Up & Scale-Out

Terminology

- Scale-up e.g. monoclonal antibodies
  - Traditional approach to creating product supply for clinical studies
  - Few product batches created at an ever increasing scale of production
  - Few manufacturing centers with national / international distribution
- Scale-out e.g. HSCT
  - Increasingly popular approach for patient-specific therapies
  - Ever increasing number of product batches created at a similar (single-patient) scale of production
  - Potential for multiple manufacturing centers with national / international distribution

- 7 -

Academic and Industry Partnerships
Process Scale-Up & Scale-Out

Scale-up versus Scale-out (excluding ultra-orphan indications)

- Phase 0/1 studies: ~12 patients
  - Single or few clinical sites within country
- Phase 2 studies: 60+ patients ± control population
  - >1 potentially 10s of sites in different countries
- Phase 3 studies: 100+ patients ± control population
  - Likely >10s of sites in different countries
- Commercialization: likely 1000's, 10,000's of patients
  - Ideally globally

- 8 -

Academic and Industry Partnerships
Process Scale-Up & Scale-Out

Types of Processes

- Typical donor or patient-derived therapy

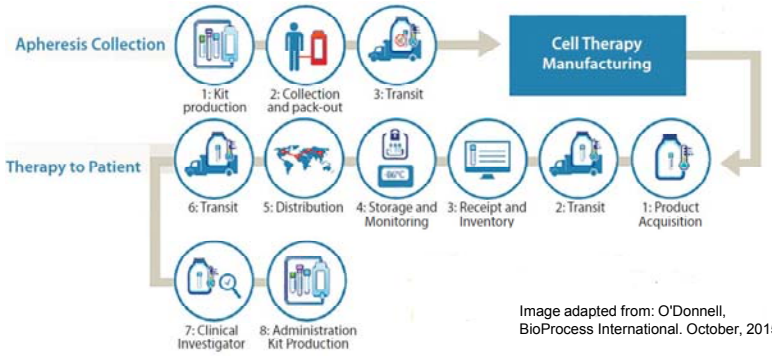

Image adapted from: O'Donnell, BioProcess International. October, 2015

- Whole process is repeated for every patient
  - Requires manufacturing scale-out, ideally with automated unit operations

Academic and Industry Partnerships
Process Scale-Up & Scale-Out

Types of Processes

- Typical highly expanded-allogeneic therapy

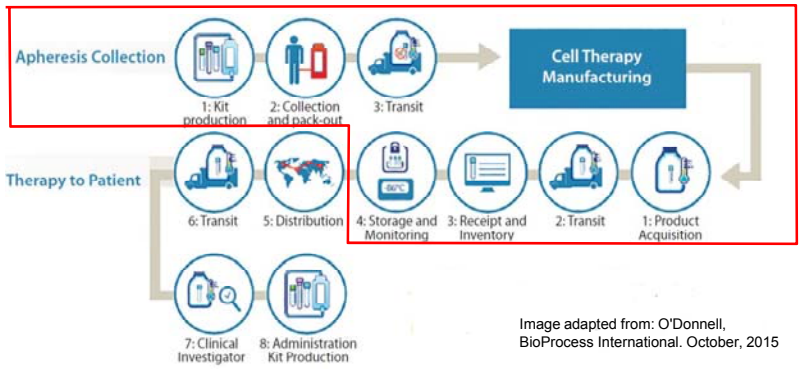

Image adapted from: O'Donnell, BioProcess International. October, 2015

- Small part of the process is repeated for every patient
  - Requires manufacturing scale-up (elements in red conducted once / few times per product life)

Academic and Industry Partnerships
Process Scale-Up & Scale-Out

Technologies (Cell-based Therapies)

- Scale-up
  - Increasing use of process analytical technologies
  - Increasing use of complex bioreactors to achieve required scale
  - Predominant use of single use disposable
  - Investment of process-development time to define CQAs to ensure scalability
- Scale-out
  - Increasingly use of automation to achieve throughput and scale
  - Increasing use of simple bioreactors to achieve scale
  - Almost complete reliance on single use-disposable systems
  - Investment of process-development time to define patient-to patient (batch-to batch) variability

Academic and Industry Partnerships
Process Scale-Up & Scale-Out

- System / Process Control
  - The ability to control a process during scaling can only be as good as the ability to measure the process
  - Measurements (QC) should define critical to quality (CQAs) attributes of the process
    - e.g. transduction efficiency, cell expansion, cell identity, product purity & functional attributes (efficacy)
  - Long-term process variation should be determined, but might be expected to be ~3x short-term variation

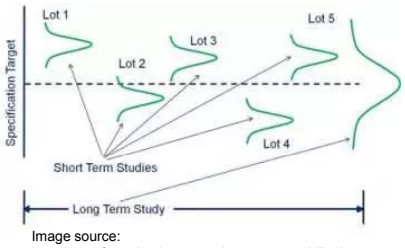

Image source:
http://www.free-six-sigma.com/process-capability.htm

Academic and Industry Partnerships
Process Scale-Up & Scale-Out

Key Considerations

	Scale-up	Scale-out
Changes in unit operations with increasing scale	Modest to major	Minor
Utilization of labor with increasing scale	Increasingly efficient	Modest efficiency gains
Cost and consequence of batch failure	Major	Minor (depending on indication)
Process development required to increase scale	Major	Modest
Quality control	Simple	Complex
Compatibility with highly complex processes	High	Low

- 13 -

Academic and Industry Partnerships
Technology Transfer Conclusions

- Ask not what your partner can do for you, but what you can do for your partner
- Each partner may have different priorities and terminologies
- Assume tech. transfer will take longer than initially expected
- TPPs are useful (start with the end goal in mind)
- The larger the scale (scaled-out or -up) the better the process understanding needs to be to control variation
- When in doubt put the patients first

- 14 -

Thank You

stewart.abbot@fatetherapeutics.com