Catalent®



Impact on Technology Integration on Better & Faster Biosimilars Pipeline

Christelle Dagoneau, PhD
Business Development Director, CATALENT BIOLOGICS

©2016 Catalent Pharma Solutions. All rights reserved

DEVELOPMENT DELIVERY SUPPLY

more products. better treatments. reliably supplied.™

Contents

1. Catalent Overview & Biosimilar Background
2. Biosimilar Landscape & Trends Analysis
3. Smart Strategy for Biosimilar Cell Line Development

1. Catalent Overview
& Biosimilar Background

Catalent Expertise with Biologics & Biosimilars

Trusted	**Proven**	**Committed**
20+ years experience in Biologics services	Partnerships with **41** of the Top 50 Biotechs	**$75M+** invested in science and technology
		
400+ antibodies, **70+** recombinant proteins developed	**43+** GPEX® cell line development programs in clinical trials	**$20M+** invested in a new biomanufacturing facility
59+ master cell banks, 83+ cGMP bulk drug batches released	**12+** biosimilar programs in PI/PIII; **7** on the market	Acquisition of Redwood Biosciences for SMARTag™ Technology
20 year track record in analytical and fill/finish programs	Analytical services provided for **25** Biosimilars	Investment in Advasept® Glass-Free Injectable Technology

Catalent Biosimilar Technology & Capabilities

Catalent GPEx® Technology

- 5 months from cDNA to high-performance clones
- No antibiotic selection, no gene amplification
- 100% of clones are stable, 2-7g/L titers
- Proven technology

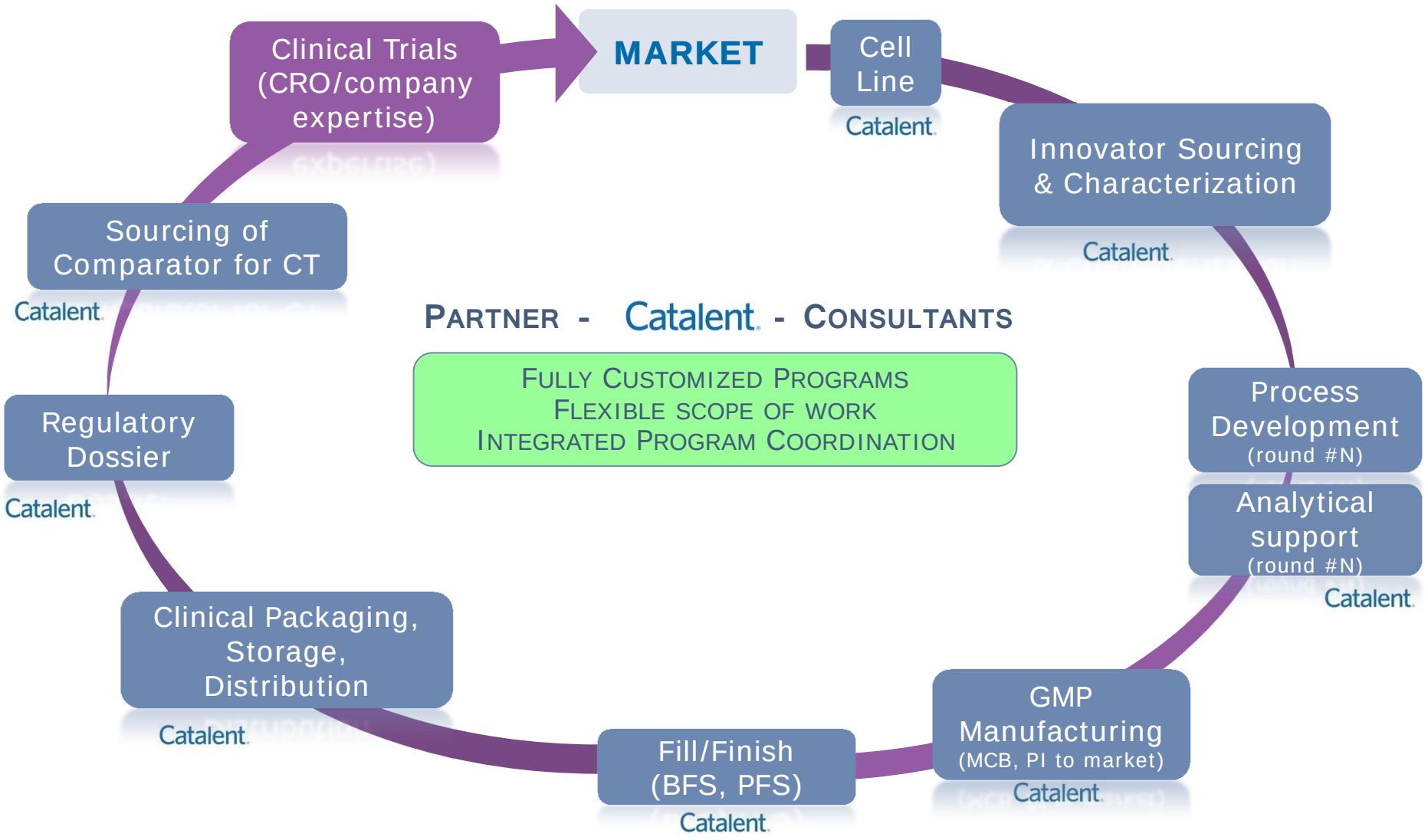
Portfolio of GPEx® Cell Lines for Biosimilar Development

- 12 cell lines available for licensing
  - Therapeutic Areas: Oncology, Asthma, Autoimmune/RA, Osteoporosis, RSV, Cystic Fibrosis, Multiple Sclerosis
  - Current development status at partners: from preclinical to commercialization
- Non-exclusive cell line agreements
- New cell lines being developed each year

Integrated Suite of Services

- Process Development; GMP manufacturing
- Comprehensive analytical services for biosimilarity exercise
- Comparator sourcing & characterization
- DS, DP testing & release; Stability studies
- Sterile fill/finish; Clinical supply; Storage; Distrbution
- Regulatory support

Catalent Partnership Approach: Tailored Solutions from Cell Line Engineering through Clinical Supply



2. Biosimilar Landscape & Trends Analysis

Biosimilars Present Global Opportunity for Growth

- Market approval is driven by regulatory guidelines
- EU has become the reference for most biosimilar developments
  - ✓ **21** products approved
  - ✓ 2nd generation: Inflectra/Remsima + Benepali
- US is behind :
  - ✓ **2** products approved
  - ✓ Sandoz Filgrastim (Zarxio™) was the 1st biosimilar approved in March 2015 (non-mAb); Inflectra in April 2016
- Estimate **700** follow-on biologics therapies in the pipeline
- Estimate **245** biopharma companies focusing on biosimilars
- Slow market uptake of biosimilars predicted in the EU because of non-interchangeability & reduced discounts on price compared to generics
- Authorized interchangeability may change the market dynamics in the US

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



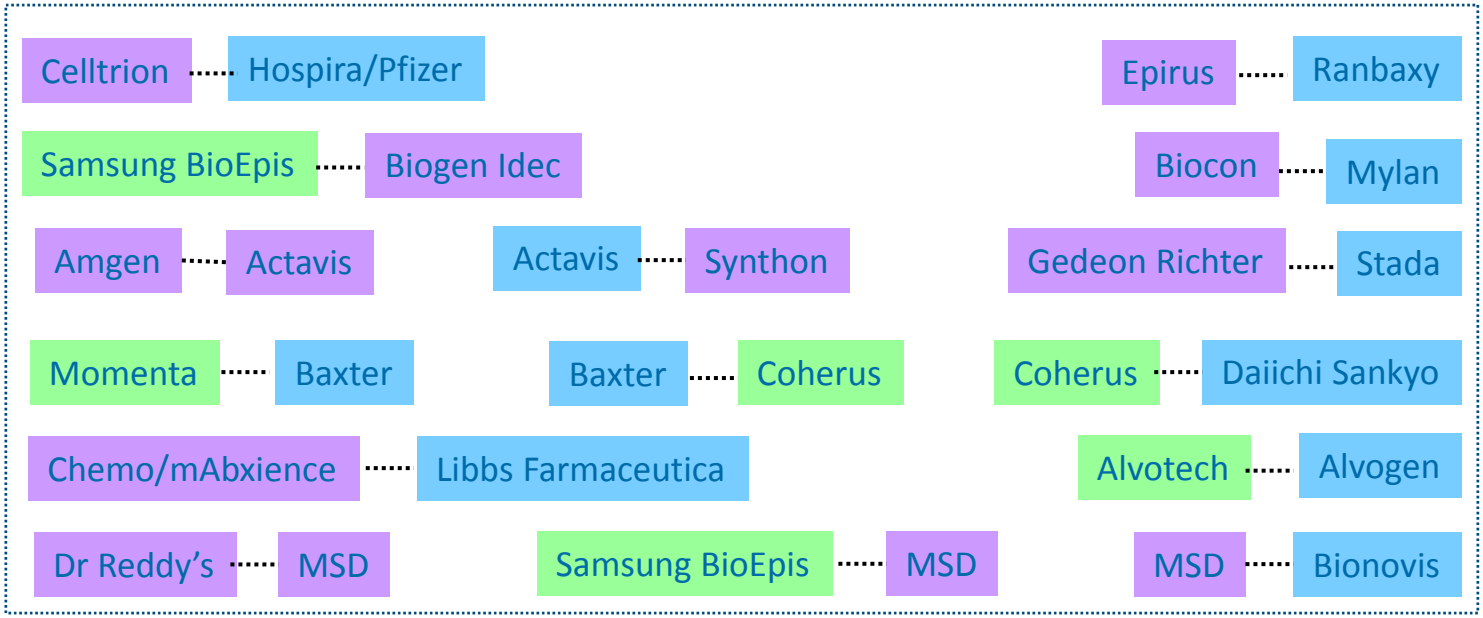
> >



FDA

Biosimilars Business Models

- Complexity of biosimilar mAb development has led to the set up strategic Development & Commercialisation Alliances



Source: 10th Annual Bioplan; biobetter/biosimilar counts from biosimilars.com

- With the uptake of the biosimilar market, more M&As are expected

February 5th, 2015: Pfizer acquired Hospira ($17 billion deal)

Development Strategies

- Numerous models based upon vertical integration from process development through manufacturing to marketing



- Common trend: <u>Outsourcing of the cell line development + Analytical assays</u>
  - CLD: Custom development and benchmarking of multiple clones from various vendors & in-licensing of specific biosimilar cell line
  - Analytics: Bioassays, complex glycosylation testing
- Rare examples of Pharma-CMO partnership: TEVA-Lonza (JV 2009-2013)
- Acquisition of Bioceros (cell lines portfolio + technology platform) by Epirus in Sept. 2015; sold to Polpharma in June 2016

Catalent Analysis of Industry Trends

New Actors Entering the Biosimilar Market

- Generic industry
- Start-up companies
- Companies supported by governmental incentives

New Business Models

- More companies starting 100% virtual – Key outsourcing component
- Flexible and strategic partnership structures
- Looking for differentiation factors: specialty markets, orphan drugs, manufacturing process, …

Technical Challenges

- Identification of the best (=high yield + biosimilar) cell line
- Relevant analytical strategy (in-house, outsourced, tech transfer)
- Maintaining low COGs

Keys to Success

Technology platforms & development path are critical to address:

- Biosimilarity
- Time to Market
- Cost of Goods

Optimal programs involve:

- Use of high-performance cell lines
- Fully integrated process development & characterization platforms
- GMP capabilities if required
- Tech Transfer support
- Wide technical & regulatory expertise (drug company, CMO, consultants)
- Full cooperation and open communication between ALL partners

3. Smart Strategy for Biosimilar Cell Line Development

Improve Biosimilar Candidates Selection

Challenges

- Biosimilarity/ functional profile are driven by host cells machinery and cell culture conditions
- Biosimilarity is difficult to predict and therefore requires intense clone screening work
- Clone screening requires combined analytical and upstream process development expertise and equipment
- Making multiple high-yield stable CHO cell lines is time consuming and costly

Solutions

- **Using a Multiplex approach and Catalent GPEx® platform to screen a wide variety of high-yield biosimilar clones**

Why is GPEx® Technology Unique and Valuable

Versatile	Works on any mammalian cell line, and many eukaryotic cell lines
High Yields	Gene inserts target “active” regions of the cell genome, allowing for high levels of antibody production from the cell pools and lines
Shortened Timelines	Antibiotic selection or traditional gene amplification is not required, resulting in shorter clonal cell line development timelines
Complex Molecules	High transduction efficiency, coupled with no antibiotic selection requirement, allows easy “titration” of multiple genes to the correct gene ratio to yield maximum recombinant protein production and efficient protein formation
Time & Cost Savings	The technology inserts each copy of the transgene at a different genomic location producing very stable gene insertions and stable expression from both pooled and clonal selected cell lines.

Integrated Analytics & Upstream Process Development

- Providing necessary information for making intelligent decision on lead clones
- Combine cell culture conditions (use of ambr) & analytics in the clone screening process
- Correlate analytics with functionality (CQAs)



Example set of analytics

- Aggregation (SEC)
- Charge Variants (cIEF)
- Glycoprofiling (stage appropriate)
- Binding (Octet specific versus non-specific)
- Potency (cell based)

Benefits:

Automation

- Consistency = higher quality data
- Staff spend more time on science

High throughput

- Many experiments in parallel (x 48)
- Reduces timelines
- Highly scalable to full bioreactor scale, 15 mL to 100-1000 L scale

Multiplex GPEx® Strategy
1 sequence x multiple HCL x CQAs

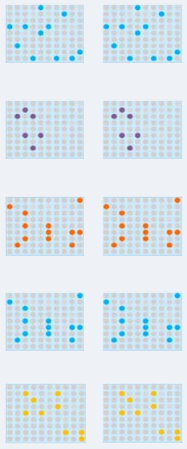
6-8 Months (hundreds to few lead candidates)

Explore multiple Host Cell Lines
- **CHO-K1**
- **CHO-S**
- **CHO-DG44**
- **HEK**
- **Etc.**

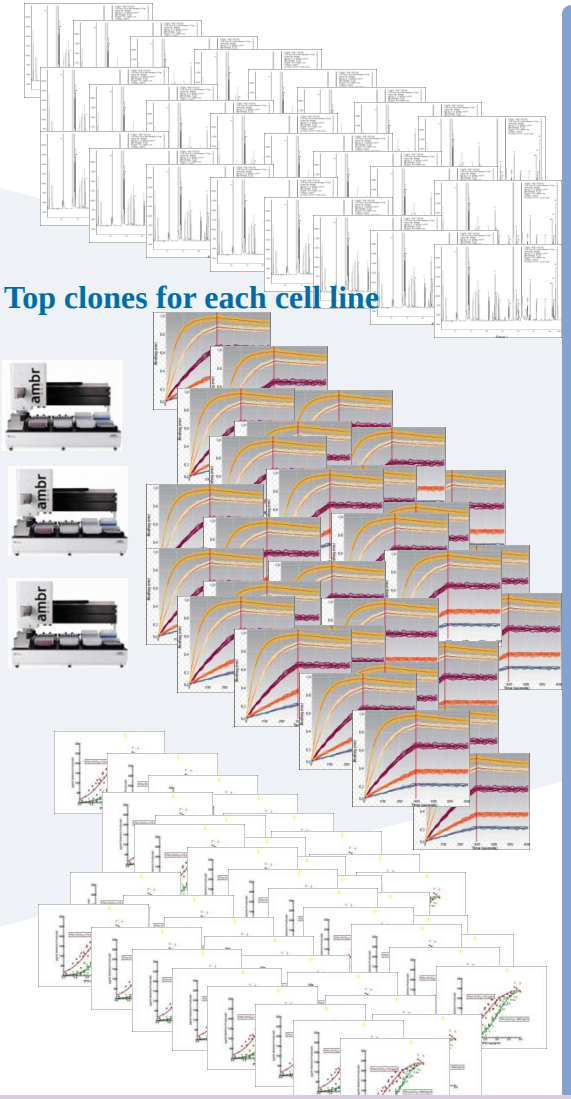
GPEX Transduction



Clonepix



Screening Clones with productivity and analytics



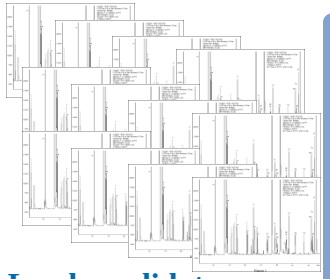
Top clones for each cell line

Narrowed Candidates

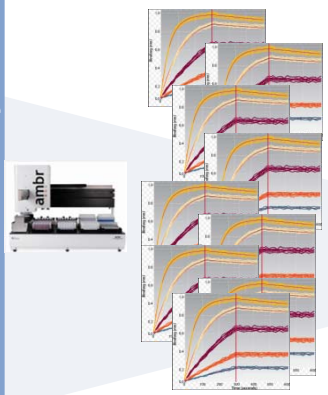


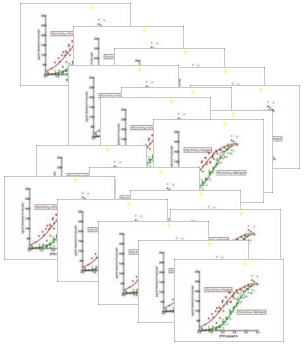
Clonepix
2nd for monoclonality

narrowed list of candidates under variety of culture conditions



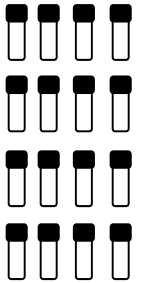
Lead candidate





Deliverables

Master Cell Bank



Project Report Inclusive of CMC required submissions for IND



Smart Clone Selection Using Multiplex Strategy



- Parallel screening of multiple clones in GPEx® high-performance production platform.
- Integration of Analytics in clone selection process
- Use of Ambr platform to screen culture conditions
- DOE: More data, better decisions in shorter period of time.
- Fast, efficient, cost effective ability to multiplex screen a wide variety of parenteral cell lines *in parallel.*

Catalent®

Catalyst + Talent.
Our name combines these ideas.

www.catalent.com

Christelle Dagoneau
+33 637 444 907
Christelle.Dagoneau@catalent.com

OSDrC is a registered trademark of Sanwa Kakagu Kenkyusho Co.
©2015 Catalent Pharma Solutions. All rights reserved.

more products. better treatments. reliably supplied.™