CMC biologics

Right. On Time.

Graham Byng, Senior Director Business Development

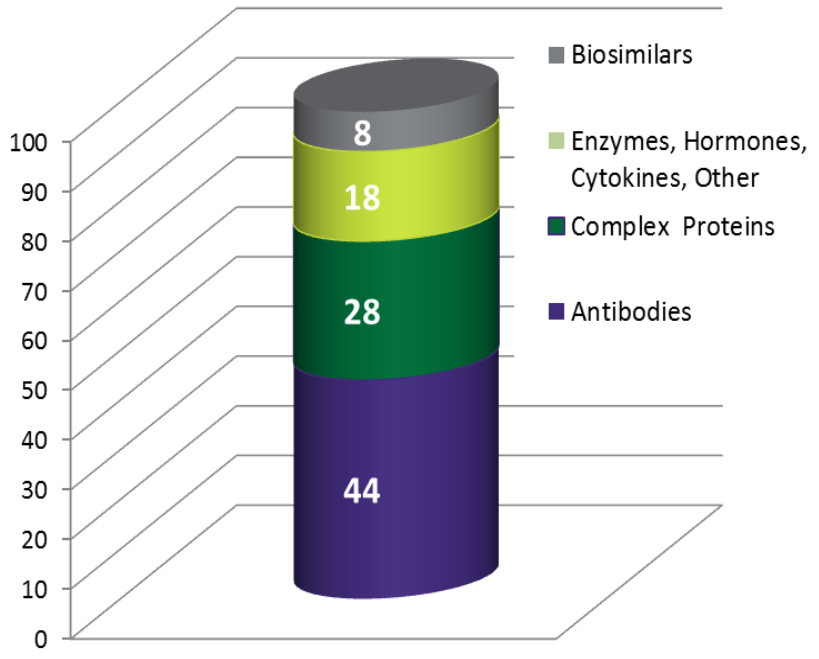
About CMC Biologics

- 15 years experience in the development and manufacture of therapeutic proteins, supplying API for toxicological and clinical trials, as well as for commercial distribution
- cGMP facilities in Bothell, WA, Berkeley, CA and Copenhagen, DK, providing clinical and commercial solutions for 85+ customers on five continents
- Focused on technical excellence, strong quality systems and exceptional customer partnerships
- Largest dedicated independent biologics contract manufacturer in the world with demonstrated track record of success and expertise
- Qualified for Commercial Production by both FDA and EMA regulatory agencies

CMC Biologics Today

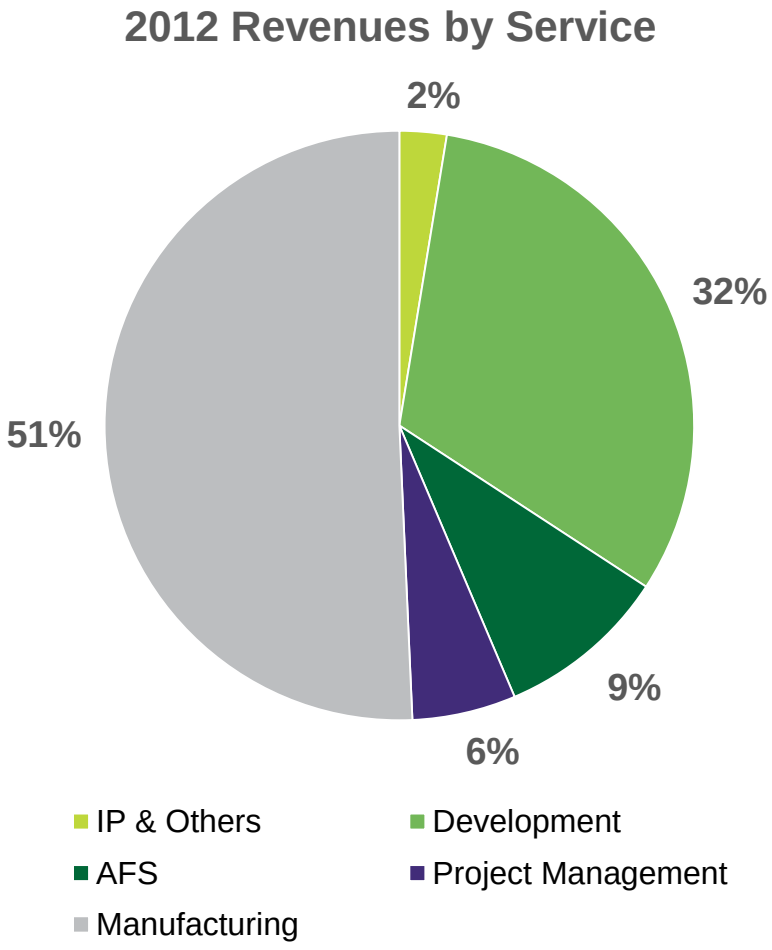
CMC Biologics is the largest independent contract development and manufacturing organization of therapeutic proteins for your clinical and commercial production globally

- 15 year track record of technical success in development and GMP manufacturing of therapeutic proteins
- World class GMP commercial manufacturing facilities, FDA and EMA compliant, in both USA and in Europe
- Leader in the implementation of technologies that accelerate our customers time to market
- Devoted to our customers' satisfaction, we have an expanding portfolio of over 85 customers in five continents

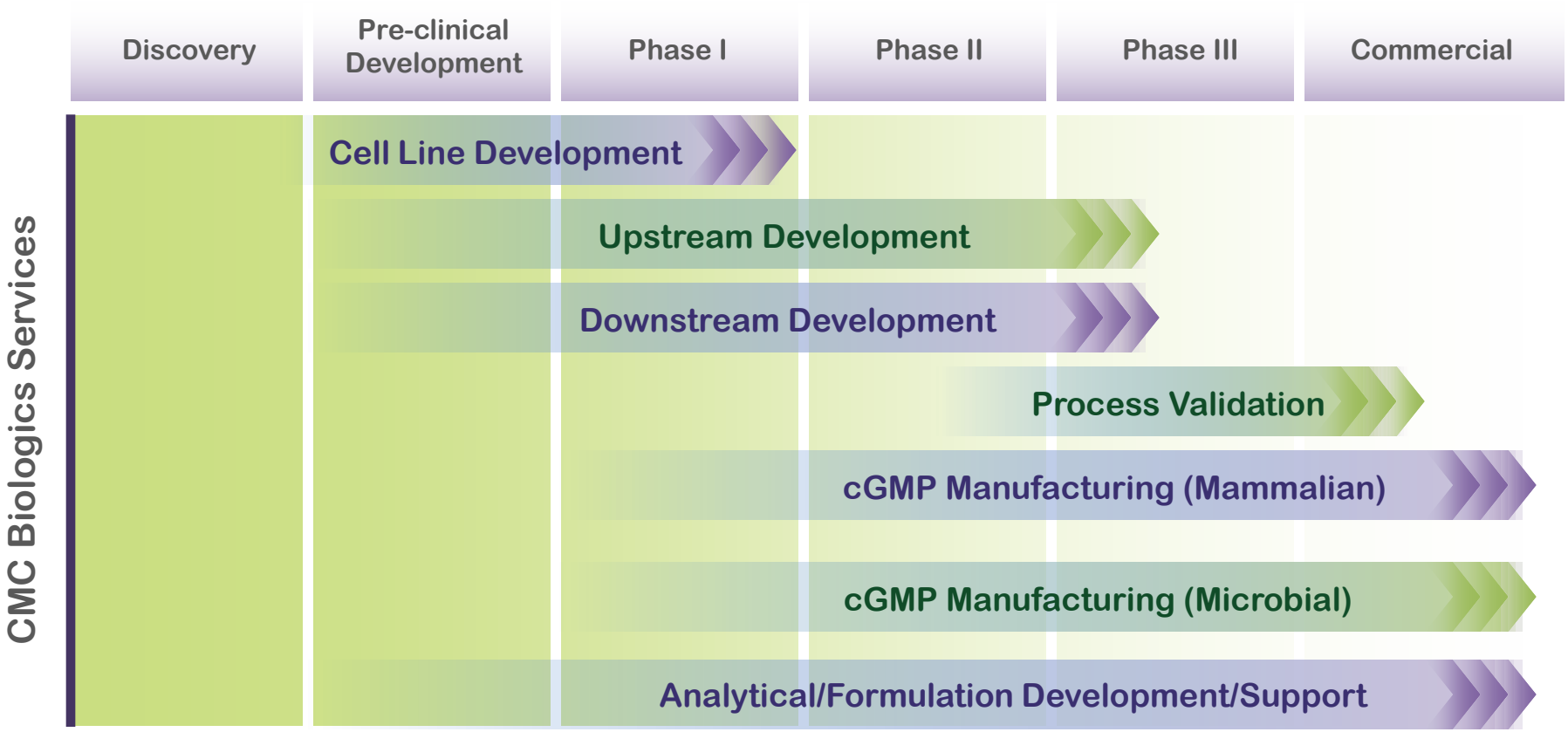


Overview of Service Offering

- **Cell Line Development**
  - Creation of cell lines, CHEF1 technology
- **Process Development**
  - Upstream and downstream process development, process characterization and validation
- **Analytical Development, Formulation Development, Stability Studies (AFS)**
- **Clinical manufacturing**
  - Manufacturing of API for tox and Phase I/II/III studies in under EMA/FDA/JP GMP
- **Commercial Manufacturing**
  - Manufacturing API for market distribution, including conformance lots under EMA/FDA/JP GMP
- **Quality Services**
  - QP release, QC testing, regulatory support



CMC Biologics Range of Services

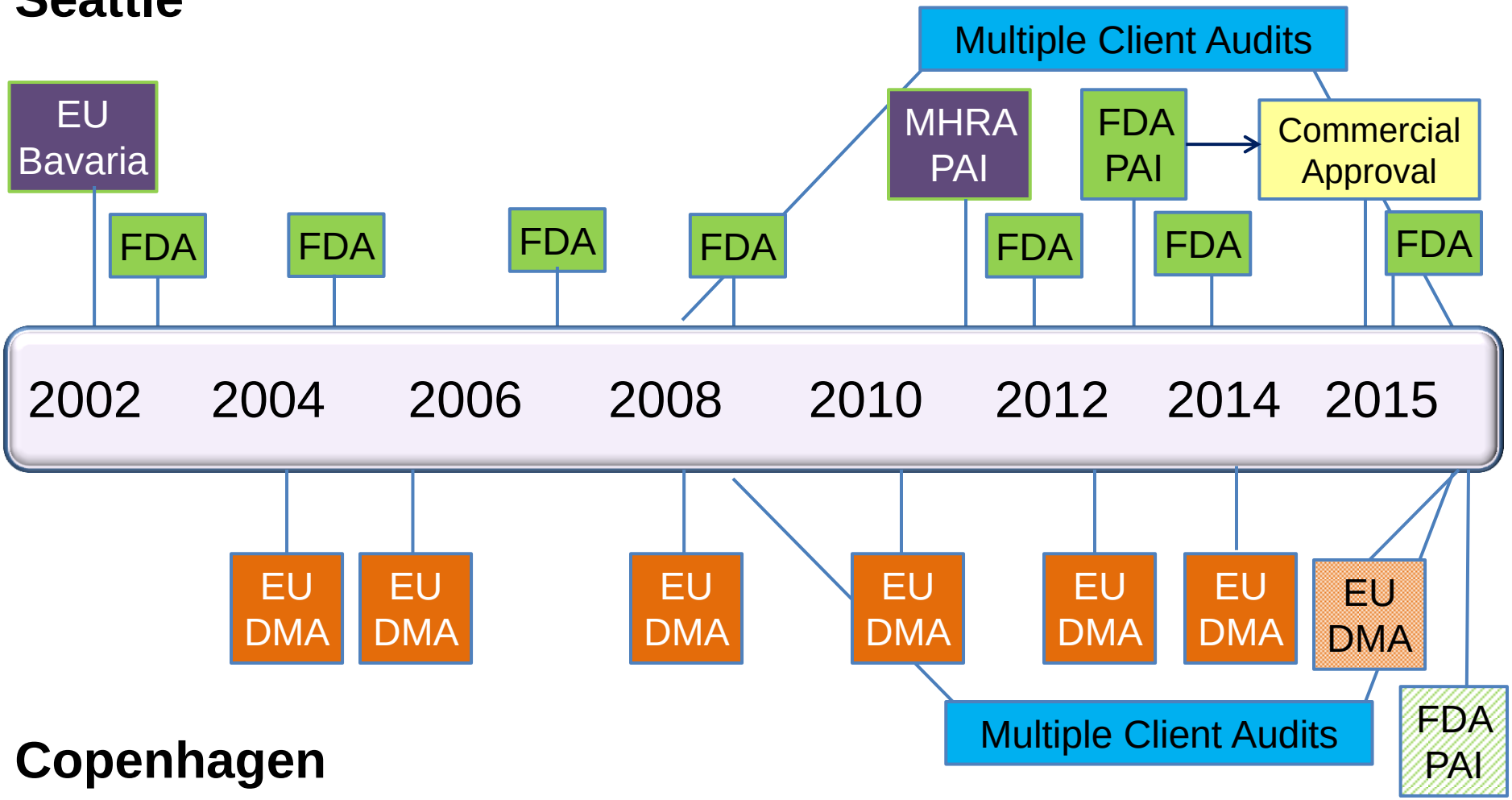


Diverse, Long-Standing Customer Base

- CMC Biologics' customer portfolio is a mix of large, mid-size and small/virtual pharma and biotech companies
- Our global customer portfolio has projects originating in the US, Europe, Asia, South America and the middle east
- CMC Biologics serves 9 of top 20 pharmaceutical companies
- 30% of our projects are in late phase or commercial stage

Our Regulatory Track Record

Seattle



Copenhagen

Global cGMP Manufacturing

Manufacturing facilities to optimize capacity and technological flexibility; fully compliant with global regulatory standards

Copenhagen, Denmark

- Upstream and Downstream development capabilities
- 3 mammalian cell culture lines from 100L to 2000L
- 2x1500L microbial line
- Danish (EMA) commercial facility authorization, FDA PAI planned in Mid-2015
- 3x2000L expanded capacity available in Q2 2016
- Center of excellence for microbial and perfusion technology

Seattle, WA

- Upstream and Downstream development capabilities
- 2 mammalian cell culture lines – 2x3000L
- EMA and FDA certified for commercial production;
- First in market 6x2000L single-use cell culture line available mid-2015
- Center of excellence for Analytical and DS/DP Formulation Development, including Bioassays

Berkeley, CA

- Early stage mammalian facility
- 3000 m^2 in one plant
- 1 cell culture line –100L to 3000L
- Expansion capacity of additional 2x3000L lines or various Single-Use Bioreactors

Seattle 6-Pack

- In May 2014 CMC Seattle was challenged by a customer to develop a plan for
- producing commercial supply of their product which was entering Phase 3
- Clinical Trials:
- The target capacity requirements as provided by the customer were based
- on 10,000L production scale.
- CMCs production scale at Seattle facility was 2 x 3000L Stainless Steel and
- 2 x 500L SUB.
- Timelines required Process Characterization and Process Validation to be
- completed by Q2 2015 to support BLA in Q4 2015.
- Process was transferred to CPH to test the “concept” in the 2000L SUB.
- Installation of 6x2,000L SUB (6-pack)

CMC Biologics 6-Pack Facility

Expansion of Copenhagen

- Installation of 3-Pack in Copenhagen
  - Design Completed Mid-2015
  - Construction on going
  - Commissioning and qualification early 2016
  - GMP ready April 2016
- Expansion of perfusion capabilities
  - Installation of 750L Bioreactors under perfusion.
- Use of single-use fermentors for microbial processes

CHEF1® Proprietary Expression Technology Advantage

- Used extensively to create clinical production cell lines, including late-phase and commercial manufacturing
- Unique features of platform enable rapid production of monoclonal cell lines
- Consistent, stable expression of proteins in rapid time-frames
- A range of licensing terms are available for pre-IND, clinical development, and commercial production

CHEF1® EXPRESSION PLATFORM SUMMARY

HOST CELLS

- Suspension adapted, serum-free CHO DG44 cells

EXPRESSION SYSTEM

- Hamster elongation factor promoter with constitutive, high-level expression
- Rapid cell-line development
- No MTX amplification
- Stable cell-line growth and productivity
- 3 g/L in 4 months from top clones

EARLY PRECLINICAL MATERIAL

- Stable expression pools in 5 weeks capable of providing >10g non-GMP material
- Scalable up to 50g from transfection pools or top clones

IND ENABLING CLINICAL MATERIAL

- 12–16 months from receipt of DNA to delivery
  - » mAb 2.012 Fast Track: 12 months from DNA receipt to 500g GMP material (see mAb 2.012 brochure)
  - » Standard Development and Manufacturing: 16 months to release of GMP material (includes engineering run)

World Class Analytical Support

Structural Analysis capabilities

- SDS-PAGE and IEF
- HPLC: SE, RP, HI and IE
- Capillary electrophoresis
- N-terminal sequencing
- HPLC Peptide mapping
- Mass spectrometry
  - Instruments: MALDI-TOF, MSD single quad, LTQ ion trap, API4000 triple quadrupole, Synapt HDMS
  - Applications: whole proteins, carbohydrates, peptide maps and process residuals
- Glycan profiling & sialic acid quantitation
- DLS and SEC-MALLS Light scattering, CD, fluorescence, FTIR

Functional analysis capabilities

- ELISA, BIAcore and ITC
- Cell-based assays

Biosimilars

- Development of Biosimilar cell lines
  - Based on strong analytical capability
  - Produced for client
- 12 Biosimilar cell lines generated to date
- 1 Biosimilar in Phase 3 trials
- 1 Biosimilar in commercial production

2015 and Beyond

- Expanded single-use manufacturing capabilities in Seattle
  - Commercial supply for BLA filing for a client and US launch of product
- Expand single-use manufacturing capabilities in Copenhagen
- Achieved FDA approval for U.S. commercial production in the Copenhagen facility
- Establish and expand in the biosimilars marketplace
- Enhance leadership position in CHEF1® expression technology platform
- Establish position as the world leader in biopharmaceutical customer satisfaction and technical acumen

Our Strengths – Why Choose CMC Biologics?

We are the largest independent CMO dedicated to development and manufacture of complex therapeutic proteins with an unparalleled track record and reputation.

15 years of experience developing over 100 molecules		Leader in implementation of manufacturing technology	Commercially approved global manufacturing facilities
	Global customer portfolio of both large and small companies	CMC biologics	Expansion capacity and technical flexibility for growth
Exceptional technical expertise	Unmatched reputation among customers and industry consultants	Top tier leadership; 85% of workforce hold a Bachelors degree or higher; 12% are PhD's	

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