Capital Markets Tutorial: Bioanalytics
Gerry Mackay, Fiona Coats
Lab Products & Services (LPS): premium supplier for Life Science research and quality control labs

~€720mn
Sales revenue 2021

17.6%
Sales CAGR\textsuperscript{1} 2016-2021

26.1%
EBITDA margin\textsuperscript{2} 2021

~50%
Recurring revenue

Portfolio includes lab instruments, consumables, software and services

1 In constant currencies  2 Excluding extraordinary items
Continuous transition to a higher growth and profitability profile for LPS

LPS sales revenue, € in millions; EBITDA margin\(^1\) in %

<table>
<thead>
<tr>
<th>Year</th>
<th>LPS Sales (€ millions)</th>
<th>EBITDA Margin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>325.3</td>
<td>16.0</td>
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<tr>
<td>2017</td>
<td>352.4</td>
<td>16.5</td>
</tr>
<tr>
<td>2018</td>
<td>380.6</td>
<td>17.0</td>
</tr>
<tr>
<td>2019</td>
<td>408.8</td>
<td>17.5</td>
</tr>
<tr>
<td>2020</td>
<td>437.0</td>
<td>18.0</td>
</tr>
<tr>
<td>2021</td>
<td>722.2</td>
<td>26.1</td>
</tr>
</tbody>
</table>

CAGR\(^2\) 17.6%

Growth drivers:
- Sales & Marketing pivot to attractive segments and regions
- Attractive portfolio mix coupled with M&A
- Launch of innovative products
- Improved brand awareness

1 Excluding extraordinary items  2 In constant currencies
Focus on attractive Life Science market and more balanced regional profile

Sales revenue share by segment, 2021 vs. 2017

<table>
<thead>
<tr>
<th>Segment</th>
<th>2017</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life Science research</td>
<td>~55%</td>
<td>~45%</td>
</tr>
<tr>
<td>Applied research</td>
<td>~45%</td>
<td>~32%</td>
</tr>
</tbody>
</table>

of which Bioanalytics
>30pp (≈14pp)

Sales revenue share by geography, 2021 vs. 2017

<table>
<thead>
<tr>
<th>Region</th>
<th>2017</th>
<th>2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas</td>
<td>~32%</td>
<td>~29%</td>
</tr>
<tr>
<td>EMEA</td>
<td>~39%</td>
<td>~29%</td>
</tr>
<tr>
<td>Asia</td>
<td>Pacific</td>
<td>~29%</td>
</tr>
</tbody>
</table>
Bioanalytics portfolio strengthens position in Life Science research market

**Total addressable LSR**¹ market, in €

- ~5.4bn
- ~1.6bn

**Strategic considerations**

- Focus on Bioanalytics to address faster growing customer and product segments
- LSR market growing mid-to-high single digit while Bioanalytics in the teens
- Higher synergies between LPS and BPS³ in LSR than in AR⁴

**Growth drivers**

- Rich pipeline of novel molecules and proliferation of biosimilars
- Digitalization across all processes, from discovery to supply
- AI and big data continue to transform the industry

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¹ Life Science research  ² Bioanalytics  ³ Bioprocessing Solutions  ⁴ Applied research; Source: Various market and analyst reports and company financials
Bioanalytical tools address pain points of Life Science customers

Developing a new drug is costly, time-consuming, and involves a high risk of failure

~€500m average costs of drug discovery

>4-5 years time required for R&D and testing

Only 1 out of 10,000 molecules make it to the market

Bioanalytics improve R&D productivity by...

...digitizing and automating key steps in molecule and cell line development

...providing customers with valuable data and analytics to make better decisions earlier in the process

...decreasing likelihood of late-stage failure, shortening time-to-clinic, and achieving better results faster

Time-to-market is key for customers: being first-in-class is more important than being best-in-class

Source: Association of the British Pharmaceutical Industry; Duxin Sun et al.: Why 90% of clinical drug development fails and how to improve it?, July 2022
Powerful solutions to enhance molecule and cell line development processes

**Molecule development**
- **Target ID | validation**
  - Incucyte SX5
- **Library screening**
  - iQue3
- **Lead selection**
  - CellCelector
- **Lead optimization**
  - Octet

**Cell line development**
- **Gene cloning & initial selection**
  - Octet
- **Clone selection**
  - CellCelector
- **Confirmatory analysis**
  - Octet
- **Cultivation & media optimization**
  - Ambr 15
- **Evaluation & characterization**
  - iQue3
Case study: Incucyte reveals biology over time for deeper insights

- More information about drug candidates
  Time-dependent effects of experimental treatments in living cell models to reduce late-stage drug failures

- More relevant testing
  Leverage advanced cell models to recapitulate physiological and pathological conditions

- Boost productivity
  Parallelize experiments with 6x more capacity than traditional approaches

Incucyte allows for deeper understanding of cellular behavior to accelerate drug discovery and research
Dive deeper into accurate and reproducible results with Incucyte
Case study: Octet reduces screening time and increases throughput

Octet BLI solutions reduce titer and CQA screening time during cell line development by up to 99% vs. traditional methods

- **Fast time to results**
  Protein titer measurements in <2 minutes

- **Rapid, detailed information**
  on molecular interactions

- **Simplified characterization of workflows**
  Robust, easy-to-use platform

<table>
<thead>
<tr>
<th>Cell line development</th>
<th>Molecule development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expansion media optimization</td>
<td>Candidate characterization</td>
</tr>
<tr>
<td>Characterization</td>
<td>Lead optimization</td>
</tr>
<tr>
<td>Clone screening</td>
<td>Library screening</td>
</tr>
<tr>
<td>Gene cloning</td>
<td>Target ID validation</td>
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</tbody>
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Case study: CellCelector picks best cells reducing time for clone selection

CellCelector integrated workflow saves 5+ weeks, compared to traditional method

- Technology for automated analysis, selection and isolation of cells
- Monoclonality verification and single cell productivity measurement on a single platform
- Workflow is saving time and costs; superior performance compared to competing methods

### Traditional workflow (8+ weeks)
- Sort & seed single cells
- Verify monoclonality
- Growth assessment
- Select & expand
- Assess titer

### CellCelector workflow (>1 week)
- Seed cells
- Automated monoclonality verification
- Automated expression & secretion analysis
Also in Advanced Therapies workflow, Bioanalytics instruments are increasingly used.

![Diagram showing workflow stages]

**Advanced Therapies customers**

<table>
<thead>
<tr>
<th>With BioA solution</th>
<th>w/o BioA solution</th>
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<tbody>
<tr>
<td>34%</td>
<td>66%</td>
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**Advanced Therapies market**

Expected CAGR 2021-2026: ~30%

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1 BioA solution: Products by top ~100 Advanced Therapies customers; 2 Global data, analyst reports
Leverage strong positioning in Bioanalytics to continuously gain share in strongly growing Life Science market

Continue expansion in North America and establish strong footprint in China

Provide workflow solutions for advanced cell models & new drug modalities (e.g. CGT)

Capitalize on strong software competence

Expand share of recurring revenue
Capital Markets Tutorial: Cell Culture Media & Chromatography
René Fáber, Hugo de Wit, Michaela Pischke
Bioprocess Solutions (BPS): solution provider for biomanufacturing

- **€2.73bn**
  - Sales revenue 2021
- **36.2%**
  - EBITDA margin\(^1\) 2021
- **~75%**
  - Recurring revenues
- **~90%**
  - Sales share biopharma

\(^1\) Excluding extraordinary items
Running ahead of initial mid-term plan in terms of sales growth and margin expansion

BPS sales revenue, € in millions; EBITDA margin in %

<table>
<thead>
<tr>
<th>Year</th>
<th>Sales CAGRs</th>
<th>BPS sales revenue</th>
<th>EBITDA margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>~14%</td>
<td>1,350</td>
<td>29.1</td>
</tr>
<tr>
<td>2020</td>
<td>~34%</td>
<td>1,783</td>
<td>32.3</td>
</tr>
<tr>
<td>2021</td>
<td>~19%</td>
<td>2,727</td>
<td>36.2</td>
</tr>
<tr>
<td>2022e</td>
<td>~36%</td>
<td>3,800</td>
<td>~36%</td>
</tr>
<tr>
<td>2025e</td>
<td>~36%</td>
<td>3,800</td>
<td>~36%</td>
</tr>
</tbody>
</table>

- Mid-term targets were increased in 01/2021 (sales) and 01/2022 (margin)
- 2019-2022 extraordinary growth driven by Corona vaccines and some customers’ changed ordering pattern
- Normalization ongoing since mid of 2022
- Strong fundamental market dynamics unchanged

1 Excluding extraordinary items  2 Based on mid-point guidance 2022  3 Based on mid-term targets up to 2025: published in 2018, updated in 01/2021 (sales) and 01/2022 (margin)
M&A strategy: adding innovation, increasing share of wallet

Enhancing relevance for Life Science customers

- Broadening cell culture media and components portfolio
- Expansion of downstream portfolio
- Strengthening of positioning in Advanced Therapies

Biological Industries, CellGenix, Xell, Albumedix, WaterSep, BioSeparations, BIA Separations, Chromatography businesses from DHR and Novasep

1 Danaher Corporation
Addressing customer needs with a strong, differentiated portfolio

Protein-based therapies
- mAbs
- Bi-/Multi-specifics
- Bioconjugates | ADCs
- Recombinant proteins and peptides
- Protein-based vaccines

Viral-based therapies
- Viral vectors for gene therapy
- Virus and viral vector vaccines
- Oncolytic viruses
- Novel modalities (e.g., mRNA, DNA, Exosomes)

Advanced therapies
- Cell therapy (e.g., iPSC, MSC)
- Gene-modified cell therapy (CAR-T)

~10% unmet needs
~20% yields
~30% robust manufacturing

Process intensification
Unmet needs
Yields
Robust manufacturing

Share of molecules in R&D pipeline; source: GlobalData, November 2022
Expected market CAGR 2021-2026, Sartorius estimates
Cell culture media (CCM) business: well positioned in an attractive market

Total addressable BPS market\(^1\), in €

- ~17bn
- ~2.2bn

Cell culture media 2021

Strategic considerations

- Leverage the leading position in upstream processes
- Media are specified into the process and part of the approval and therefore difficult to replace
- Recurring revenue with attractive gross margins

Growth drivers

- Media market expected to grow in line with the modalities of the biopharma market
- Focus on faster growing Advanced Therapies
- Demand increases as drug candidates move through clinical phases, continuous demand after approval

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\(^1\) Sources: GlobalData, Citeline, Alliance for Regenerative Medicine and BCC Research; Sartorius estimates
Chromatography business: recent acquisitions significantly strengthened BPS’ positioning

Total addressable BPS market\(^1\), in €

- ~17bn
- ~3.2bn ➔ Chromatography

2021

Strategic considerations

- Chromatography an essential step in purification of biopharmaceuticals
- Sartorius’ purification offering broadened through “classical” plus innovative assets
- Focus on intensified chromatography and cell & gene therapies

Growth drivers

- Healthy and strong pipelines of novel modalities
- Growing need for process intensification in mAbs and biosimilars
- Strong positioning of monolith and membrane technologies & strategic portfolio fit for intensified market

\(^1\) Sources: GlobalData, Citeline, Alliance for Regenerative Medicine and BCC Research; Sartorius estimates
Extensive synergies in CCM’s sales and manufacturing network

Cross-selling synergies within existing portfolio

- CHO cell line
- Cell line development
- Bioreactors
- Fluid Management
- BIA monoliths

Synergies within cell culture media operations

- **Biological Industries**
  - manufactures own portfolio and media portfolio of CellGenix

- **CellGenix**
  - supplies growth factors and cytokines as raw material for BI\(^1\) media production

- **Albumedix**
  - supplies and produces critical components for BI\(^1\) and CellGenix media

- **Xell**
  - produces HEK and CHO portfolio

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1 Biological Industries
CCM trend #1: regulatory requirements for GMP grade critical raw materials

When new modalities start to enter the clinic phases, there is a need for regulated quality products and regulatory support to obtain approval

Research / discovery / development phase
- Use RUO\(^1\) media and additives
- No need for regulatory advice/support
- Focus on efficacy getting the treatment to work

Clinical trials / market supply phase
- Need for FFM\(^2\)/cGMP\(^3\) media and additives, DMF\(^4\)
- Need for regulatory understanding to file and obtain approval for trials and market
- Beside efficacy focus on safety and quality

1 Research Use Only  2 Fit for Manufacturing use  3 current Good Manufacturing Practice  4 Drug Master File
Case study CellGenix: regulatory know-how and state-of-the-art products support accelerated approval

Customer situation
- Customer develop new therapies in their laboratories for many years
- Regulatory requirements ask for safety and quality assurance beside efficacy before allowing clinical trials
- This means switching materials, repeating pre-clinical studies or delayed start of trials to comply with regulations

Sartorius solutions
- Enable safe, efficient and consistent manufacturing of cell & gene therapies and accelerated market approval
- Regulatory support for specific customer requests and/or respective regulatory agency (EMA¹, FDA², PMDA³)

1 European Medicines Agency  2 Food and Drug Administration (U.S.)  3 Pharmaceuticals and Medical Devices Agency (Japan)
CCM trend #2: new platforms for safe and reliable raw materials

Innovative technology platforms enable the replacement of animal and human sources for critical raw materials, increasing safety, quality and affordability.

Customers’ challenges using animal / human serum

- Contaminates from human/animal source
- Batch to batch variability
- Limited supply

Sartorius solution

- Safe recombinant source
- Defined quality, proven batch-to-batch consistency and controlled manufacturing
- Scalable supply
Case study Albumedix: enabling safer, scalable access to high quality and affordable critical raw material

Customer situation

- Current commercial manufacturing for a vaccine developed decades ago
- Design and use of suboptimal manufacturing processes, using animal and human sourced material with risks of process carry-overs, batch to batch variability and high cost

Sartorius solutions

- Next-generation, serum-free, highly purified vaccine manufactured using serum-free media and recombinant rather than serum-derived excipients
- Result: vaccines stay therapeutically effective, safer, more affordable and stable, enabling distribution in more than 100 countries, including most of Asia and Africa
CCM trend #3: scaling-up solutions for new modalities

Especially for new modalities there is limited process know-how and scalability available, which is required for an efficient and economic market entry.

<table>
<thead>
<tr>
<th>New modalities process development</th>
<th>New modalities manufacturing</th>
</tr>
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<tbody>
<tr>
<td>• Focus on getting the process to work in the lab</td>
<td></td>
</tr>
<tr>
<td>• Limited experience and manufacturing expertise available</td>
<td></td>
</tr>
<tr>
<td>• Focus moves to Cost of Goods</td>
<td></td>
</tr>
<tr>
<td>• Need for access to scalable process solutions</td>
<td></td>
</tr>
<tr>
<td>• Need for access to production know-how</td>
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</table>
Case study Biological Industries: combination of innovative products with scalable manufacturing solutions enables fast access to market

Sartorius combines media know-how and supply with proven solutions to freeze and thaw liquids in bags

Customer situation

- Started to use stem cell media selected on performance
- Supply of frozen media in bottles
- Larger quantity of media to be supplied in bags, once scale-up starts and moves to manufacturing scale
- Challenge to freeze/thaw bags in a consistent manner
- Solving the problems can be time-consuming and delay clinical trials

Sartorius solutions

- Celsius system, specifically designed for the controlled thawing and freezing of the bags containing liquid media
- Result: fast, scalable, robust solution, that supports short timelines towards clinical production at high and stable quality
Chromatography trend #1: from batch production to intensified processing

- Batch
  - Limited productivity
  - Larger production footprint
  - Higher resin consumption

- Intensified processing
  - 10x higher productivity
  - 3x less footprint and CAPEX
  - Higher product quality, less batch-to-batch variability
Levels of intensification in downstream processing

**Level 0**
- Standard batch standalone unit operation

**Level 1**
- Intensified, standalone unit operation: increases the individual step productivity; less resin usage; improved buffer management

**Level 2**
- Connected process: at least two process steps; subsequent steps start before first step is finished; software orchestration is beneficial

**Level 3**
- Continuous process: highly integrated connected process; steady-state flow; software orchestration is a must; long running times; closed processing
Sartorius’ solutions for intensified processing

Process intensification leads to >10-fold higher productivity & saves up to 30% cost in clinical process

Resolute BioSMB
- Continuous chromatography systems
- Single-use flowpath
- Scalable

Resolute BioSC
- One system combines up to 3 process steps
- Low footprint

PD
Process 80/250
Pilot
Case study large pharma: BioSMB improves footprint, productivity and flexibility at reduced costs

Before: single-column batch Protein A chromatography

- Column diameter: 40 cm – larger footprint and requires a lot of storage space
- Resin volume: 20L – Protein A one of the most expensive steps in downstream
- Specific productivity: 16g/L/h

Conversion to single-use multi-column Protein A step

- Resin volume: 3.85L, 80% reduction of protein A resin
- Reduction in overall cost
- Specific productivity: 56g/L/H
Chromatography trend #2: from multi-use, resin-packed columns to single-use chromatography devices

**Membranes**
- High processing speed, high productivity
- High purification performance for new drug modalities
- Plug & play: ready-to-use formats, single use

**Monoliths**

**Resins**
- Column packing & cleaning validation
- Large equipment footprint
- Less applicable to large biomolecules like viral vectors or plasmids
Sartorius’ solutions for high performance chromatography in novel and demanding applications

- Single-use alternative to Protein A resins
- 20x higher productivity
- >30% cost reduction in clinical manufacturing

CIMmultus

- Unique high performance technology
- Specifically optimized for purification of new modalities, e.g. viral vectors, mRNA, plasmids
- Single-use and reusable options
Case study monoliths: scalability and robustness, high purity and yield

Molecule type
Adeno-associated virus AAV

Challenge
Achieving a scalable and robust separation of full from empty viral capsids with high purity and yield for multiple AAV serotypes

Sartorius BIA Separations products
- CIMmultus SO3
- CIMmultus QA
- PATfix

Key benefits
- Higher capacities than resin-based columns, due to large size channels, high flow rates with low pressure drops and high surface accessibility of binding sites for AAVs
- Downstream processing time reduced by 60%
- Significantly improves the recovery of AAV
- Plug & play cGMP formats, scalable from 0.05mL to 40L

Business result
- Integration of Sartorius BIA Separations’ technologies into customer’s cGMP facility (50L to 500L)
- Customer added a monolith-based process to its purification toolbox
- Included in customer’s advanced analytical toolkit for process & product characterisation
Leverage global customer base by seeding new innovative products

Building relevance and significant share in new modalities

Continuously combining existing and acquired portfolios to create innovative solutions

Media and chromatography businesses contribute to differentiation and recurring revenue