

Inspiring Advances in Bioprocessing

John Cummings

Sales Manager – Emerging markets



September 2022

 REPLIGEN

Repligen addresses needs for efficient, single-use, flexible bioprocessing

Repligen products are used in the Top 20 Pharma companies worldwide

41%

5-year
CAGR

Bioprocessing
innovator with
technology-leading
products

37%

CAGR in new
modalities

Diversified
customer base
across all biological
drug modalities

9

M&A Deals
since 2017

Growing through
innovation
acquisitions,
market strength

8

Disruptive
technologies since
2017

Drives innovation,
first-to-market
position, market
leadership

#33

Fastest growing
company
in the world

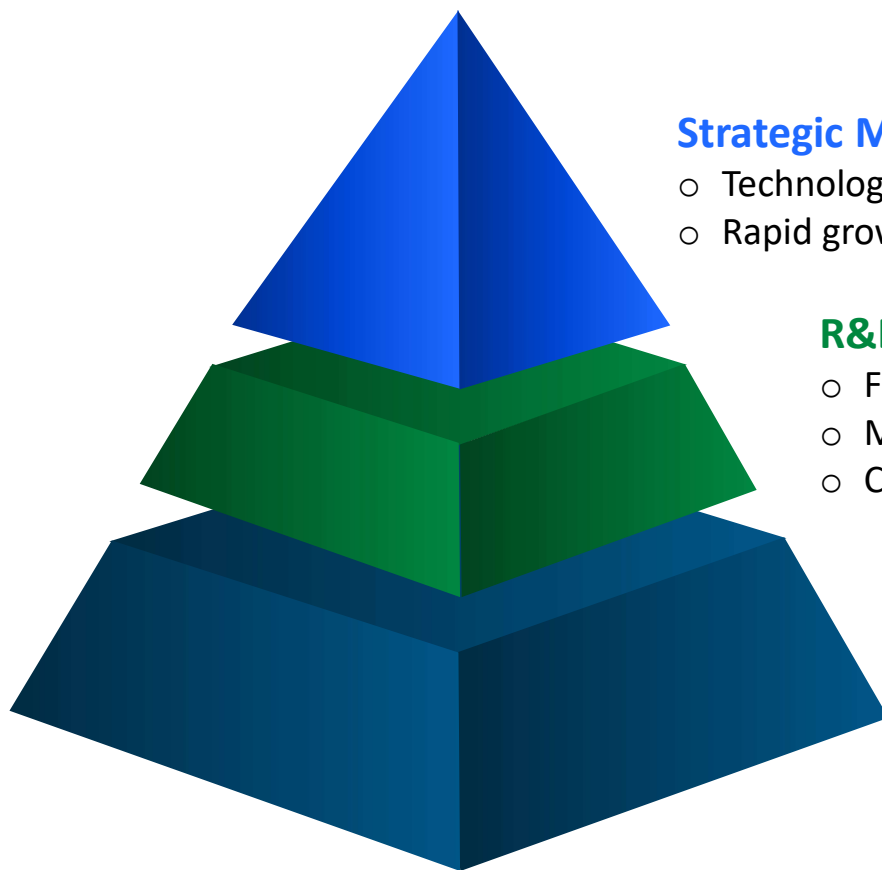
Fortune 2021

18 global facilities

2000+ employees

Enabling efficient, single-use, flexible manufacturing of biological drugs and providing first-to-market solutions for bioprocessing challenges

We have the right blueprint for continued success



Strategic M&A

- Technology Focus
- Rapid growth of acquired companies

R&D Innovation

- First-to-market product introductions
- Market-leading technologies
- Collaborations with industry leaders in key growth areas

Operational Excellence

- Capacity expansion, multi-site manufacturing
- Global commercial footprint

R&D fuels first-to-market innovation and technology leadership

First-to-Market

8
disruptive launches
since 2017



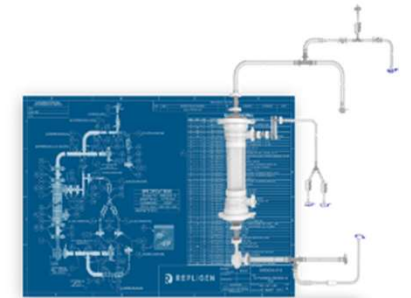
Technology Leadership

- Perfusion & process intensification
- Harvest/clarification
- Pre-packed columns
- Viral vector process optimization
- Best-in-class affinity ligands
- In-line process analytics

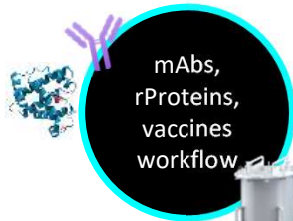


Key Partnerships

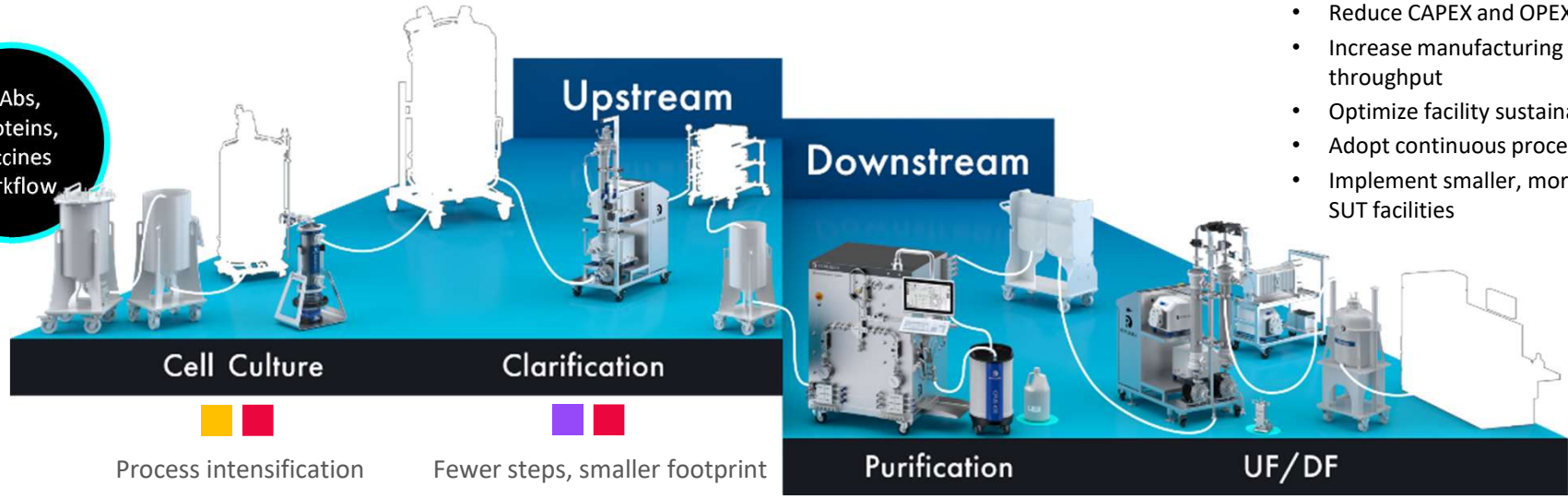
- **Navigo Proteins GmbH**
High performance affinity ligands
- **Purolite**
Next-generation Protein A resins
- **Oxford Biomedica**
Viral vector manufacturing with TFD[®]



Intensify traditional recombinant protein workflows



mAbs,
rProteins,
vaccines
workflow



- CHALLENGES:**
- Reduce CAPEX and OPEX
 - Increase manufacturing throughput
 - Optimize facility sustainability
 - Adopt continuous processing
 - Implement smaller, more flexible SUT facilities

TRENDS: Process intensification Fewer steps, smaller footprint

Scalability, flexibility, process monitoring

Rev 25Sep2022

  XCell ATF® Technology	  KrosFlo® TFD® Systems	  KRM™ Chromatography Systems OPUS® Columns	  Ligands and resins	  KrosFlo® TFF Systems Spectrum® Hollow Fiber Filters TangenX® Cassettes	  ProConnex® Flow Paths ProConnex® Fluid Management	  Solo/FlowVPX® Analytics
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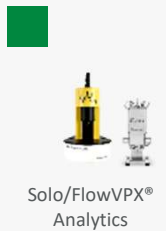
Advance the development and manufacturing of gene therapies



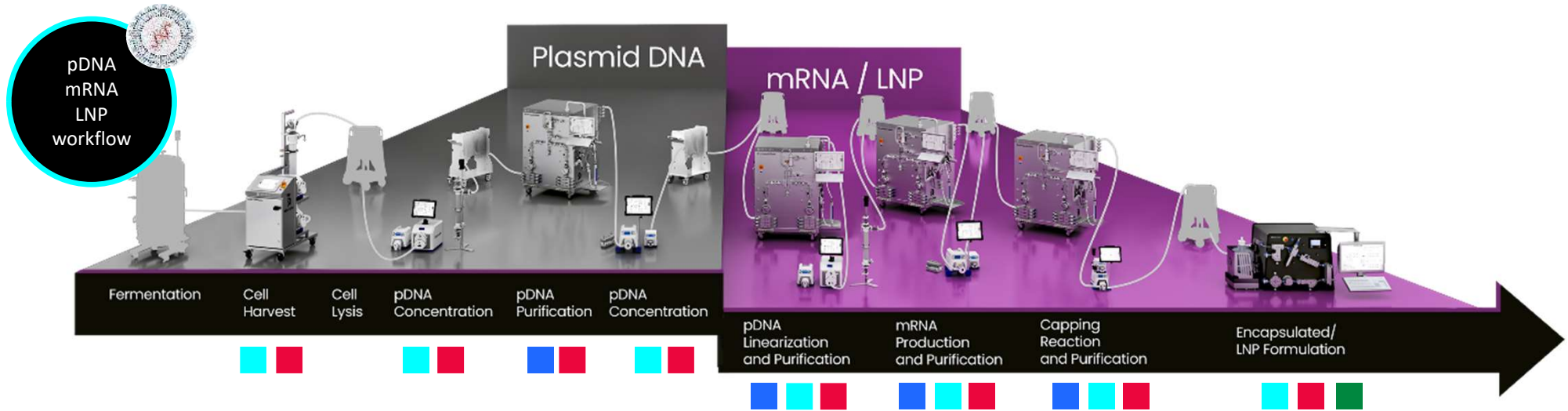
CHALLENGES:

- Commercial viability
- Surging demand
- Limited process knowledge
- Speed to market

Rev 25Sep2022



Accelerate mRNA / LNP production





Rev 25Sep2022



KRM™ Chromatography Systems
OPUS® Columns

KrosFlo® TFF Systems
Spectrum® Hollow Fiber Filters
TangenX® Cassettes

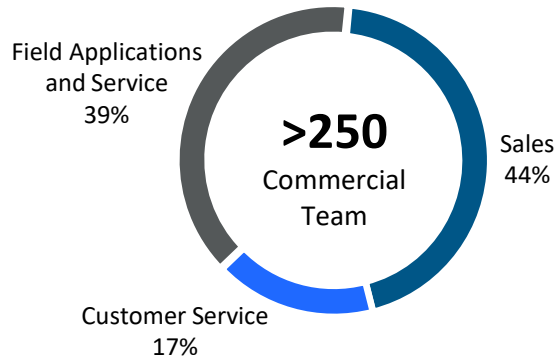
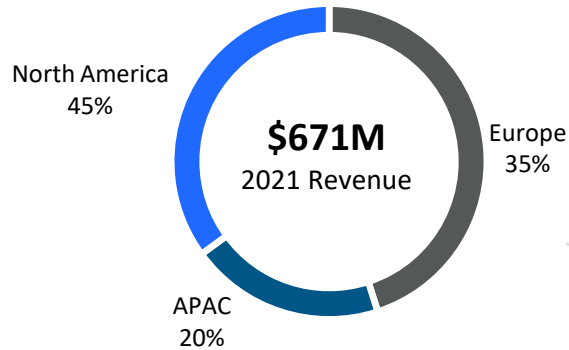
 

ProConnex® Flow Paths
ProConnex® Fluid Management

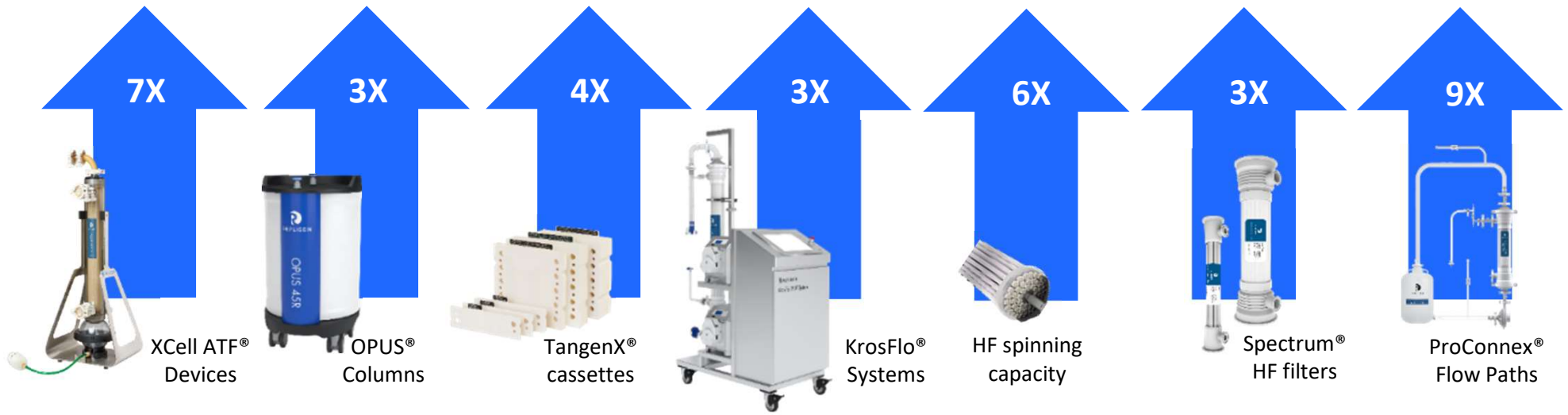
 

Solo/FlowVPX®
Analytics

Growing our presence in the world of bioprocessing



Capacity investments and progress drive best-in-class lead times

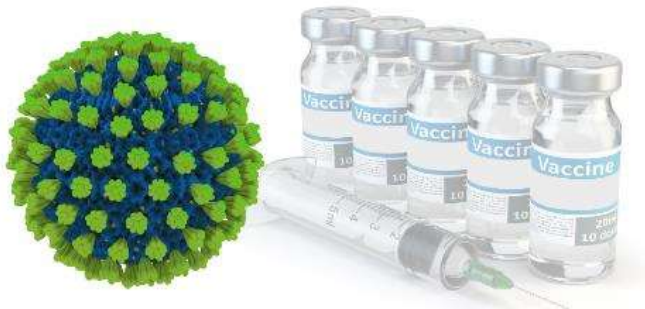


Capacity increases 2020/2021: ~\$70M investment

- Provide best-in-class lead times
- Drive business continuity through multi-site manufacturing
- Secure the supply chain
- Invest in expansion and facility improvements

Partnering to accelerate the COVID-19 global pandemic response

Repligen products are currently used in COVID-19 diagnostics and therapeutics



URGENT NEEDS

Speed to market / short lead times on key products

Improved process economics

Efficient implementation, single-use, closed systems

Scalable solutions

Dedicated, focused support, technology expertise



READY TO PARTNER AS TECHNOLOGY LEADER IN THERAPEUTICS PRODUCTION

Rapid response with COVID-19 accelerated lead times

Proven technologies with broad customer base from clinical to commercial = reduced risk

Adoption in diverse platforms including mAbs, proteins, viruses, plasmids, AAV, Lentivirus, mRNA



PROVIDING HIGH IMPACT SOLUTIONS WITH PRIORITY SUPPORT

Expert-guided priority support for rapid technology implementation

Leading technologies for upstream process intensification, downstream processing, process analytics

Closed, single-use bioprocessing – single-use, Gamma-irradiated, fully integrated flow paths


Scalable platforms supporting benchtop process development to production scale manufacturing

Inspiring advances in Gene Therapy

Technology breakthroughs and solutions for plasmid and viral vector manufacturing

REPLIGEN SOLUTIONS

FROM **GENE** TO **THERAPY**



 REPLIGEN



TECHNOLOGY AND MARKET LEADERSHIP IN GENE THERAPY APPLICATIONS

Strong market penetration with ~20% share in Gene Therapy accounts and ~150 customers

Significant technology adoption with ~50 customers at \$100K and 8 customers at \$1M in annual sales

Broad customer base including pre-clinical to Phase III candidates, CDMOs, therapy developers, academic/hospitals

Adoption in diverse technology platforms including plasmids, AAV, Lentivirus, mRNA, CRISPR, CAR-T



WORKFLOW SOLUTIONS FIT FOR GENE THERAPY

Novel solutions for upstream process intensification, downstream processing for plasmids, viral and non-viral vectors

Closed system bioprocessing – single-use, Gamma-irradiated, fully integrated flow paths

Scalable platforms supporting benchtop process development to production scale manufacturing

Dedication to Quality – ISO 9001:2015 manufacturing

Team of experts ensures rapid start-up and robust operation in GMP processes

Remote and in-person support and FAT provided

Local Sales Specialists

Experienced account managers with deep industry background act as one point of contact for customers

Field Application Specialists

Technical experts provide membrane hardware design optimization, and post-sales support for scale-up

Bioprocess Systems Specialists

Seasoned specialists with application, design and automation knowledge supporting large system projects

Project Managers

Dedicated Project Managers that act as a single point of contact for managing a project from concept to delivery, if needed

Automation and Process Engineers

Software engineers with application knowledge that support system connectivity with other unit operations, if needed

Field Service Engineers

Field-based engineers professionally trained for optimal start-up and post-sales support

Minimize downtime by leveraging expertise of well-trained specialists



Repligen-guided implementation and service ensure success

From consultation to execution

Field applications support

Consultation

- Theory
- Technology fit
- Experimental plan

Evaluation

- Demonstration
- Training
- Data analysis

Development

- Optimization
- Flow Path Sizing
- System Sizing

Implementation

- Scale-up
- Validation
- Long-term training plan

Field service support

Installation and start-up

- Installation Qualification (IQ)
- Operational Qualification (OQ)
- Operator training

Post-installation

- Extended Warranty
- Preventative Maintenance Programs
- Corrective repair, spare parts
- Service depots for rapid access to spare parts and personnel

Global support



Focus on business continuity, quality systems, and risk mitigation

Multi-site Manufacturing



Waltham, MA –
Headquarters

18 manufacturing
facilities

Stringent Inventory Management Program



Safety Stock Program

Secure Raw Material Supply Chains



Raw material and
finished good safety
stock programs

Qualified suppliers

Complete Regulatory Support Packages



Supports customer
filings

Product certifications

Hands-on Service and Support



Field Applications team
for pre- and post-sales
support

Field Service team for
equipment maintenance
and service

Committed to sustainability

Advancing our ESG strategy across 4 pillars

November 2021

Runner Up for
Best 1st Time Report

SASB & GRI Core frameworks



Focused on DE&I and Recycle/Reuse/Reduction Programs

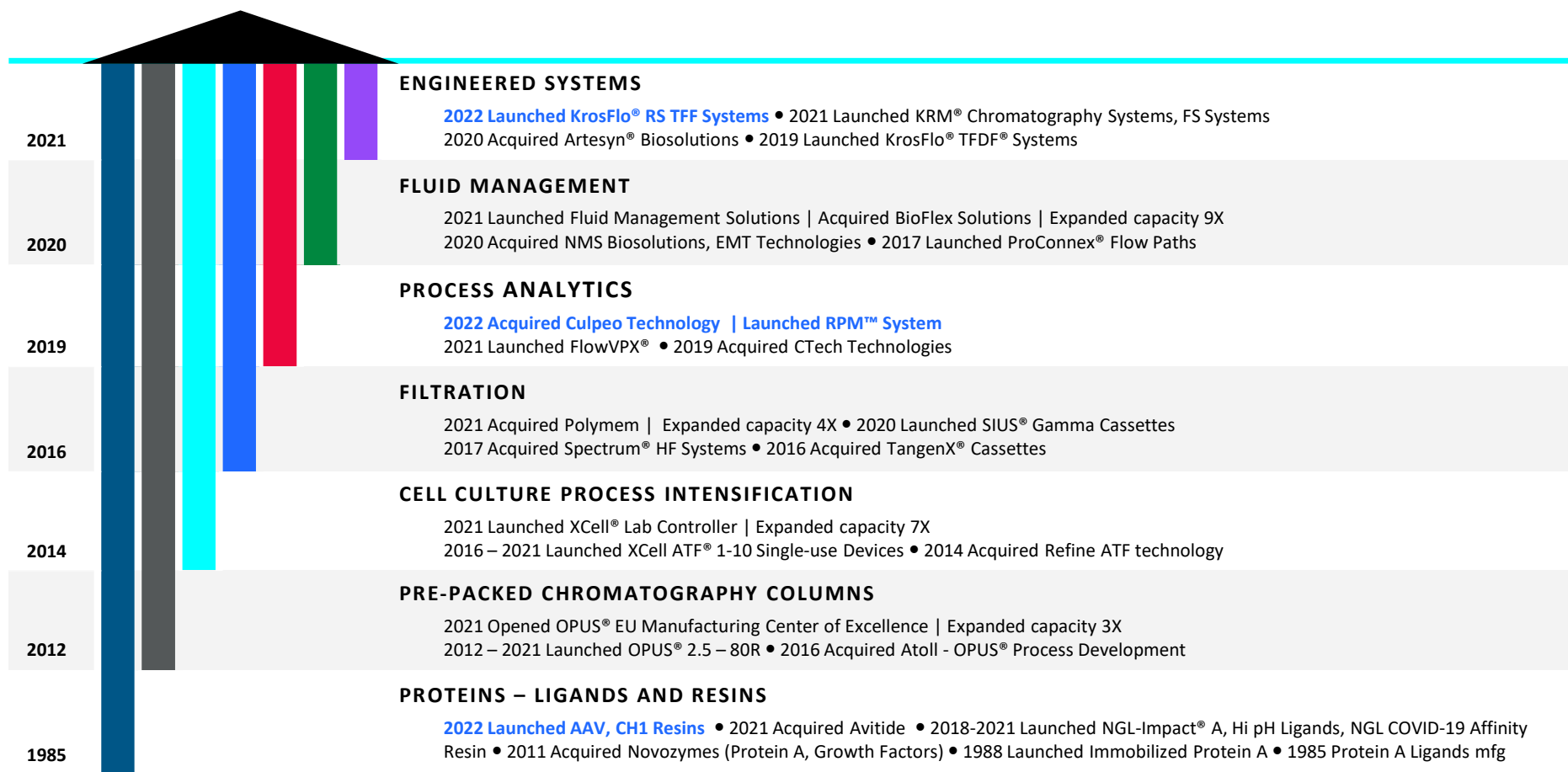
- Progressing on senior level diversity hiring objectives
- Advancing HBCU and BSCP* relationships (underrepresented student career development and internships)
- Converting machined to molded components - waste reduction
- Reducing chemical solvents in manufacturing
- Attained 100% renewable electricity at 3 additional sites (7 total)
- Advancing post-customer product recycling pilot (US and EU)
- Evaluating grey water re-use program for multiple sites

*Biomedical Science Careers Program



Rapid growth through innovative launches and strategic acquisitions

2017 – 2022 | 9 strategic acquisitions, 8 disruptive technologies



Thank you



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 **REPLIGEN**



Appendix

OPUS® Pre-packed Chromatography Columns

OPUS® 2.5 – 80R Manufacturing Scale



Configurable

Select column size and bed height to meet application-specific needs



User-specified resins

Select from > 150 resin options



Ultimate flexibility

Unpack resin using innovative side port on OPUS® 45R, 60R, 80R Columns



Leader of the pack in resin choice and size

OPUS® PD Pre-packed Chromatography Columns

Leader of the pack for bench-scale chromatography



Convenient

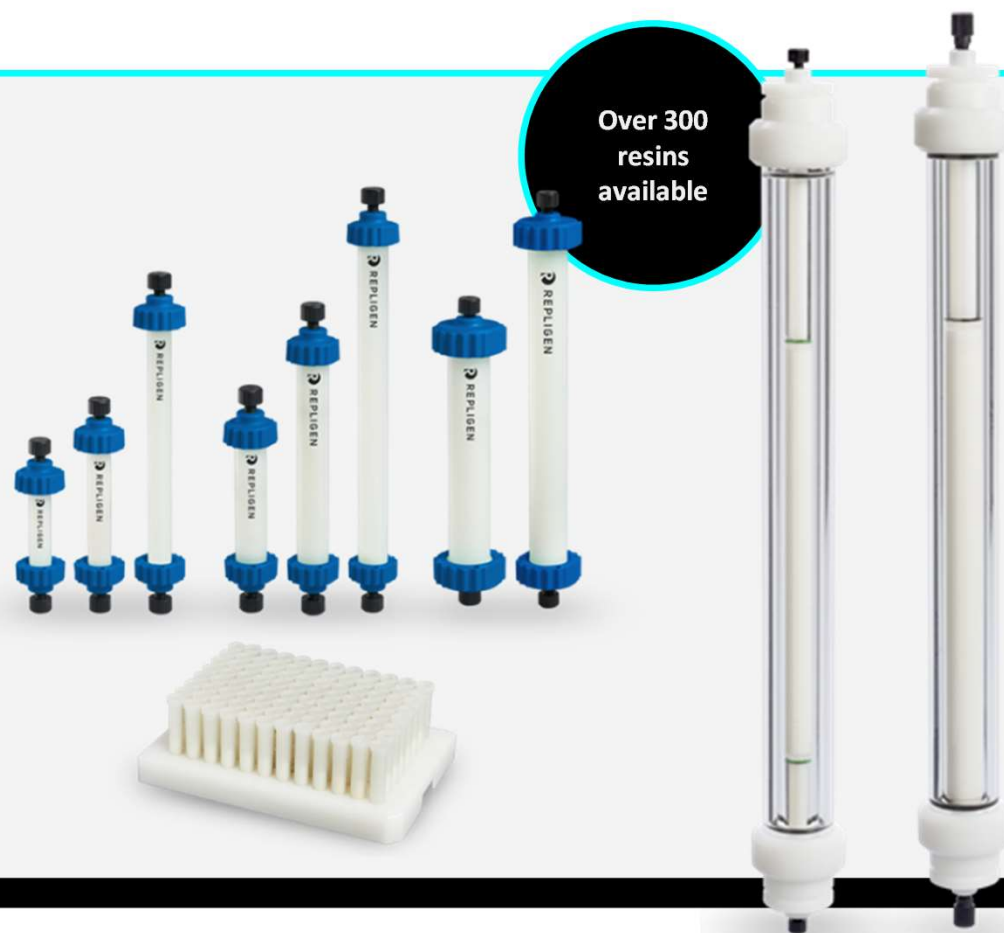
Pre-packed columns provided ready to use

- OPUS® RoboColumn® Columns for automated parallel chromatography
- OPUS® MiniChrom™ Columns for process development and sample preparation



Ideal for process validation

- OPUS® ValiChrom® Columns are exact scale-down models of full-scale columns to 1mm



XCell ATF® Cell Retention Devices

High density cell culture and process intensification devices



Technology leading performance

- 100% cell retention, high cell concentration
- Process development to commercial manufacturing



High impact applications

Perfusion, N-1 Perfusion, High Performance Harvest

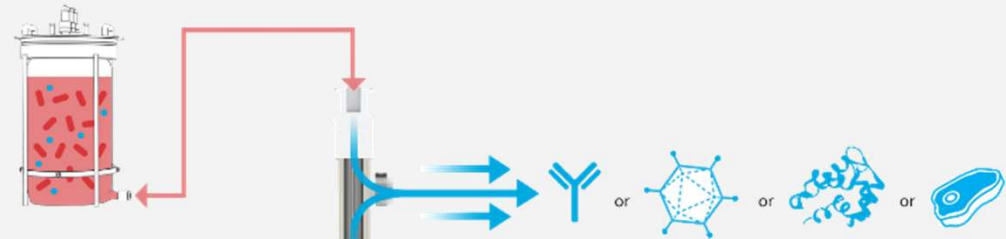


Continuous

Enables continuous processing, provides clarified harvest ready for capture chromatography

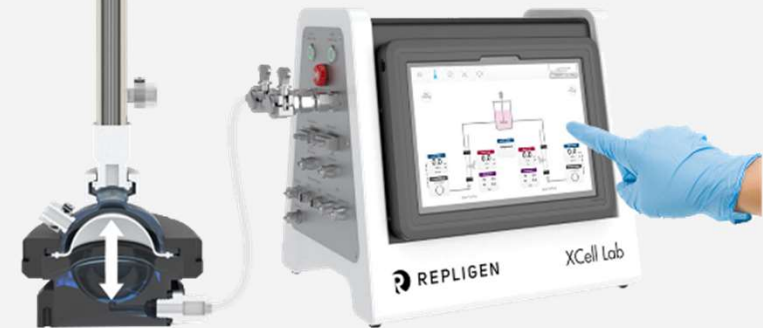


2 Formats
Single-use or
Stainless steel



**More cells.
Faster.**

**More product.
Faster.**



KrosFlo® TFF Systems – Hollow Fiber

TFF for ultrafiltration and diafiltration



Integrated system

Includes filters, pumps, process monitors, software and graphic display on a single skid



Custom flow path

Ready-to-operate ProConnex® Flow Paths – customized, configurable, complete assemblies



Scalable

1 – 5000L volumes, from process development to commercial manufacturing



KR2i



KMPi



Plex



KPS



KTF

KrosFlo® RS TFF Systems – Flat Sheet

Precision-engineered high recovery TFF systems



When every drops counts

- Minimal hold-up volumes with valve block technology
- Intelligent mixing with the lowest working volume
- Innovative tulip tank technology (RS 30 - RS 50)



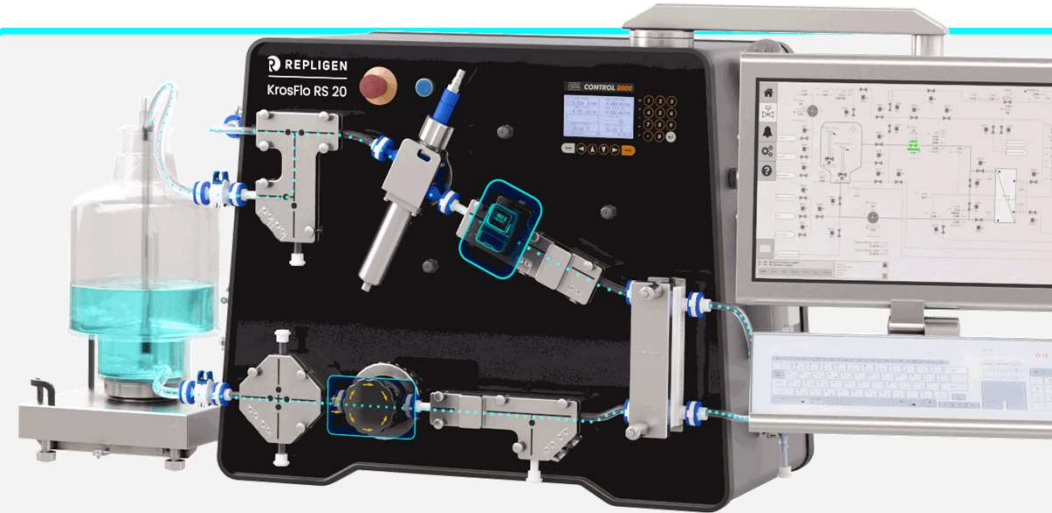
Zero human intervention

True end-to-end automation from sanitation to CIP



Scaling without compromise

Shared software, hardware, controls and cGMP compliance built into every system



RS 5



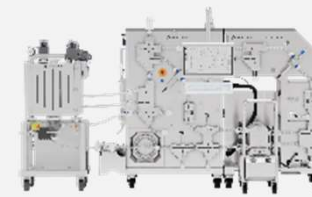
RS 15



RS 20



RS 30



RS 40



RS 50

KRM™ Chromatography Systems

Engineered for superior recovery, bioactivity and risk mitigation



Increase recovery

- Protect gradient integrity for improved resolution
- Reduce dead volume up to 4X



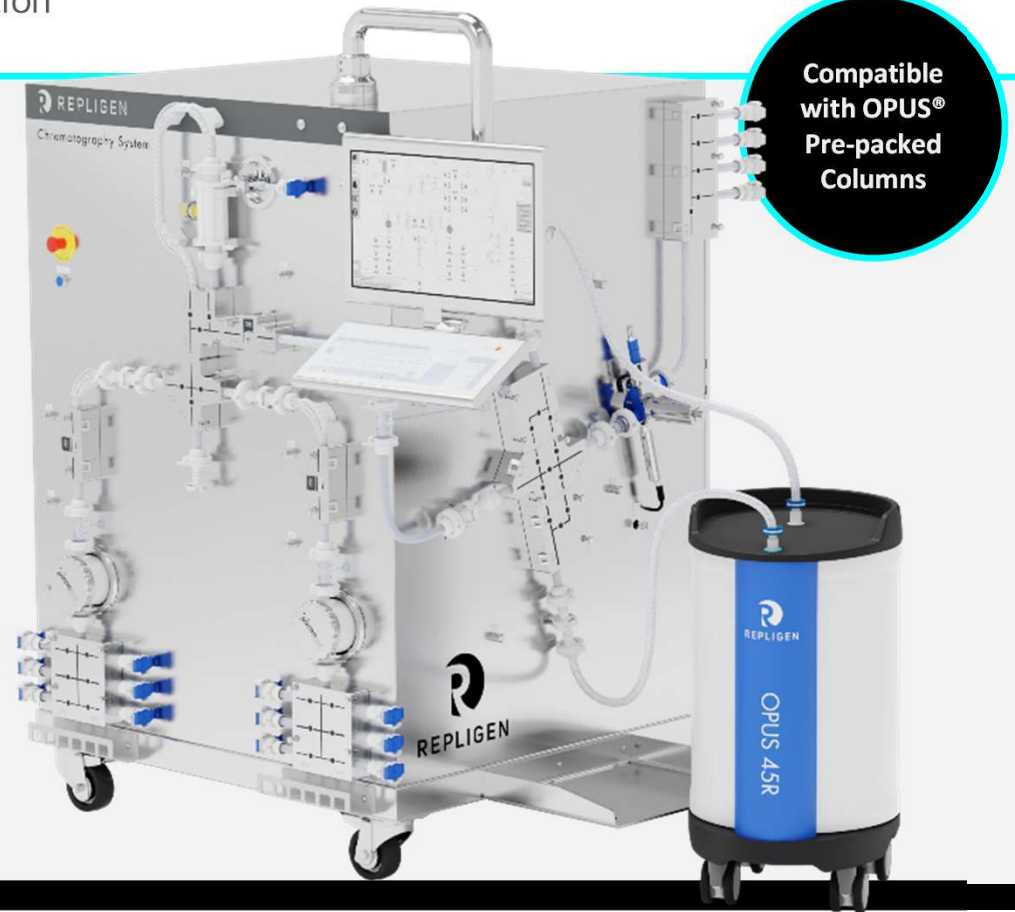
Maintain bioactivity

- Replace hose barbs with over-molded tubing connections
- Cut down mechanical stress (including shear stress)



Reduce deviations

- Mitigate risk with closed aseptic flow kits
- Make 3 simple AseptiQuik® connections and start
- Minimize human error and contamination



KrosFlo® TFDF® Systems

Combines the power of tangential flow with depth filtration



Technology breakthrough: TF + DF = TFDF®

- Unites the benefits of tangential flow (TF) and depth filtration (DF)
- Closed single-use solution



Scalable to 2000L, small footprint

Process development to commercial manufacturing



Walkaway automation

Complete dedicated solution with hardware, software, single-use flow path

Enables upstream process intensification for viral vectors



AVIPure® Affinity Resins

Innovative NaOH recyclable affinity resins based on unparalleled ligand diversity



Catalog affinity resins

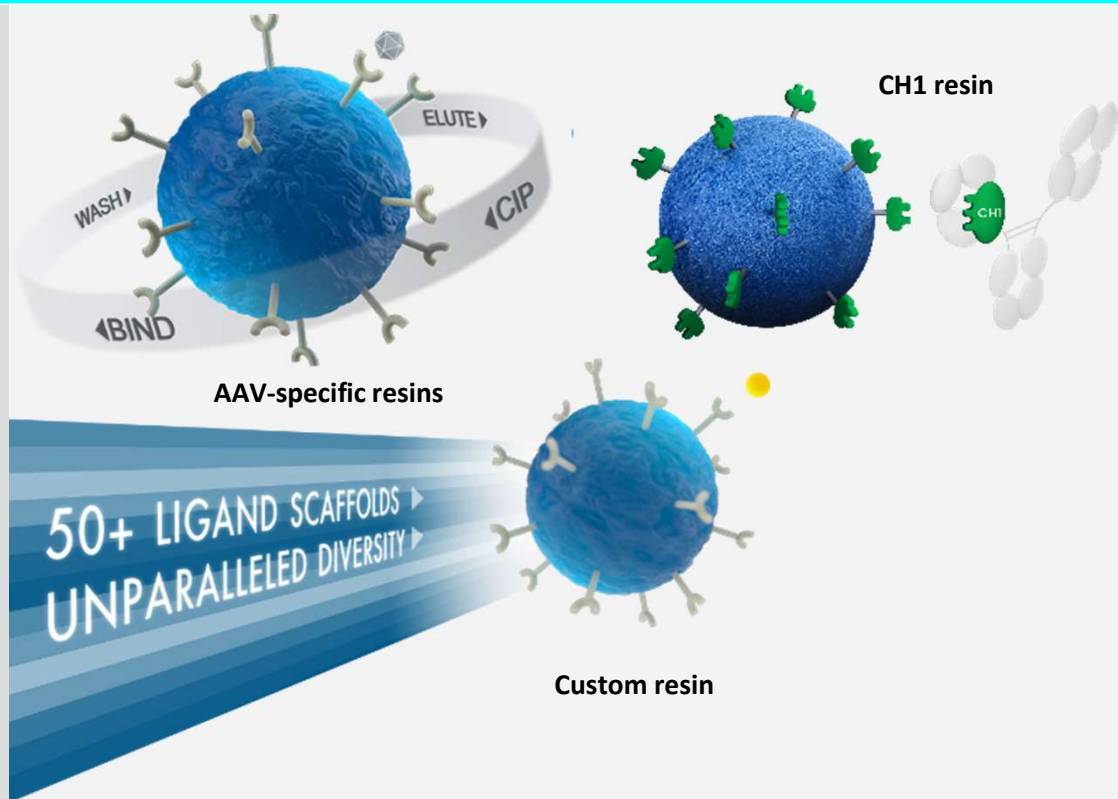
- AAV 2, AAV 8, AAV 9 Affinity Resins
Serotype-specific, NaOH recyclable
- CH1 Affinity Resin
2X capacity, clean in place with 0.1 M NaOH



Custom affinity resins

- 100% discovery success rate
- Based on 50+ ligand scaffolds
- Stable in NaOH

Available
pre-packed in
OPUS®
Columns



TangenX® TFF Flat Sheet Cassettes

High performance ultrafiltration and diafiltration



Technology leading TFF cassettes

- SIUS® Single-use cassettes
- PRO Reusable cassettes
- HyStream and ProStream membranes
- ProConnex® Flow Paths



Scalable

Process development to commercial manufacturing



Unparalleled savings – Single-use

- 50% reduction in labor cost
- 75% reduction in buffer use
- 80% reduction in filter cost

Compatible
with all
cassette
holders



TangenX® SIUS® Gamma Closed TFF Cassette

Closed, single-use system for modern concentration and buffer exchange



Superior TFF

Up to 30% more flux with multiple MWCOs, surface areas, chemistries, screens



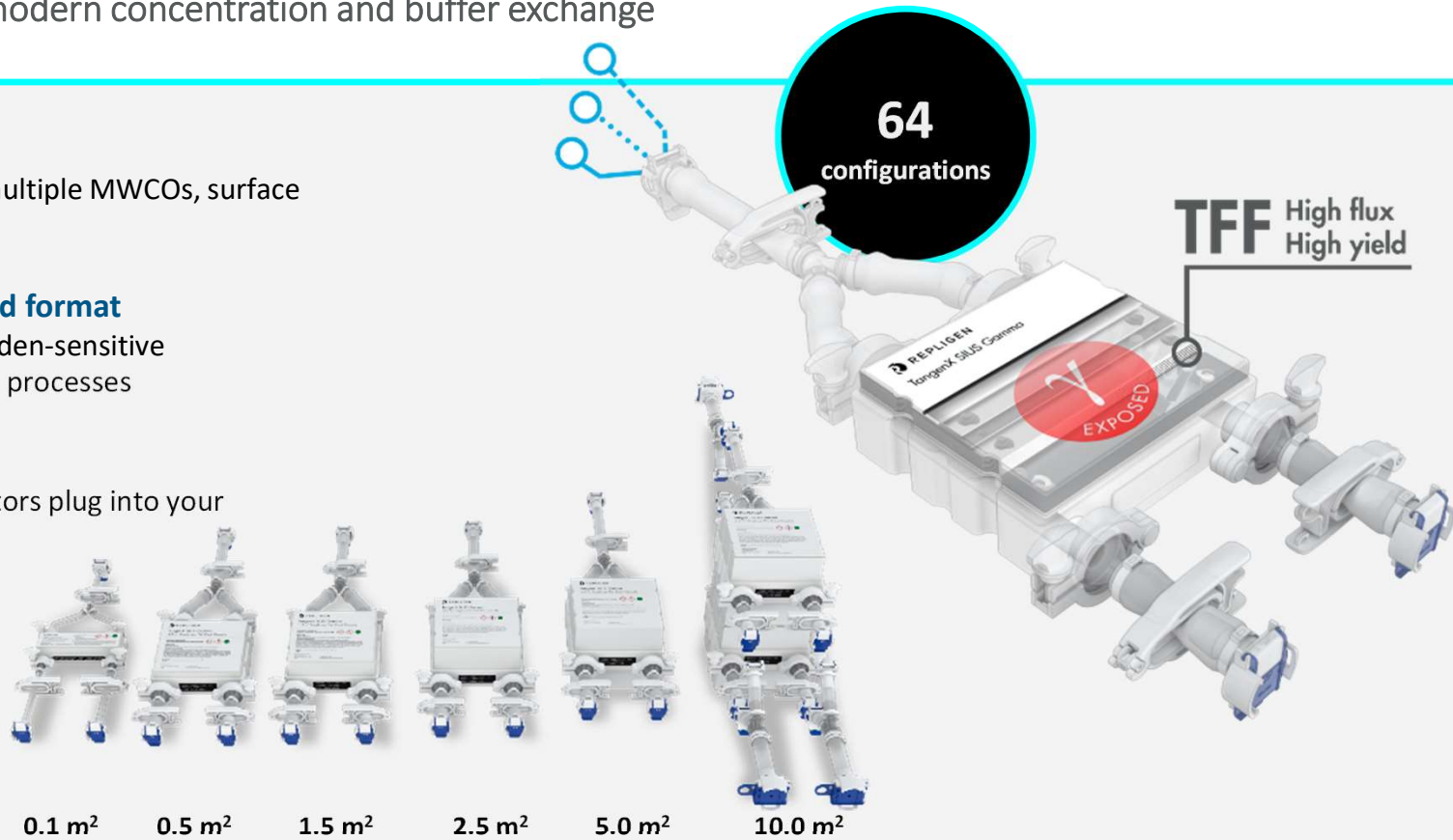
Closed, Gamma-irradiated format

Fit for gene therapy, bioburden-sensitive applications, and hazardous processes



Connection freedom

Genderless, aseptic connectors plug into your existing flow path



Surface area

0.1 m²

0.5 m²

1.5 m²

2.5 m²

5.0 m²

10.0 m²

KrosFlo® KR2i TFF System

Turnkey benchtop system for completely automated TFF



Fully integrated

Includes filters, pumps, process monitors, software and graphic display



Configurable

ProConnex® custom flow paths, 4 filter module configurations, 4 membrane chemistries, 3 effective filter lengths



Walkaway automation

Konduit add-on module for automated process value indication for conductivity, UV and temperature

**KF COMM 2
Software
13 modes of
operation**



Repligen Hollow Fiber TFF Filters

7 filter modules, 4 membrane chemistries



Broad range

- Selection of sizes, surface areas, membrane chemistries
- Process development to commercial manufacturing



High yield

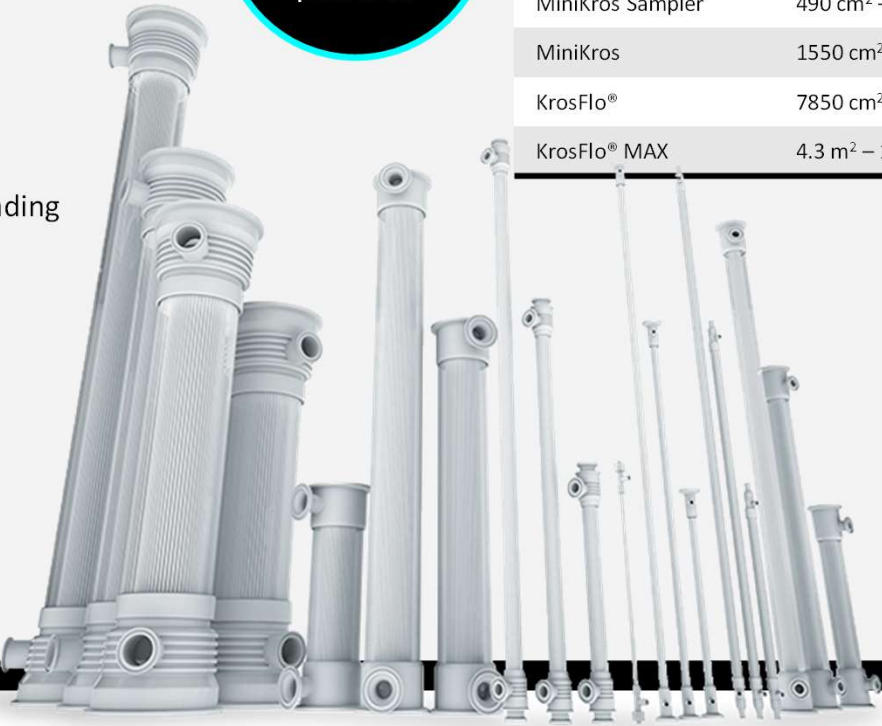
Fast processing, high flux rates, low protein binding



Compatible

For use with standard industry hollow fiber TFF systems

1400 configurations
1kD – 0.65 µm pore sizes



Filter module	Surface area	Volume
MicroKros	13 cm ² – 60 cm ²	1-100 ml
MidiKros	75 cm ² – 370 cm ²	100 ml - 3 L
MidiKros TC	75 cm ² – 370 cm ²	100 ml - 3 L
MiniKros Sampler	490 cm ² – 2600 cm ²	3 L -15 L
MiniKros	1550 cm ² – 8500 cm ²	5 L - 50 L
KrosFlo®	7850 cm ² – 4.1 m ²	10 – 100L
KrosFlo® MAX	4.3 m ² – 12.8 m ²	100L – 1000+L

ProConnex® Flow Paths

Customized, configurable and complete assemblies for tangential flow filtration

Single-use assemblies designed according to customer specifications



Configurable

Customizable flow path engineered to meet process requirements



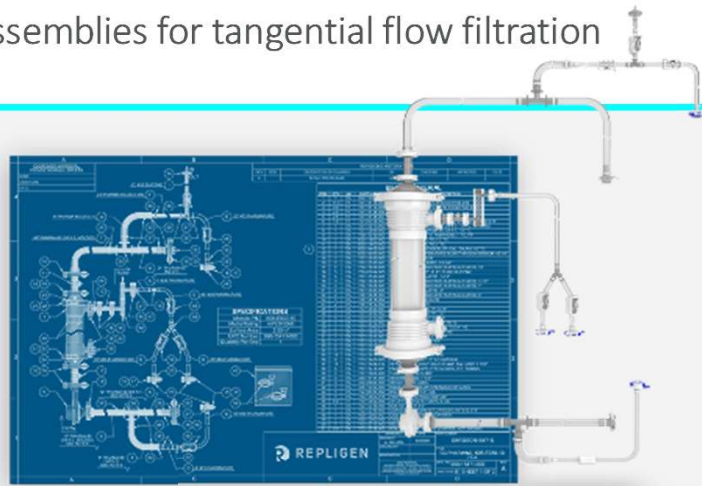
Closed, Gamma-irradiated

Convenient, ready-to-use hollow fiber or cassette filter assembly



Complete

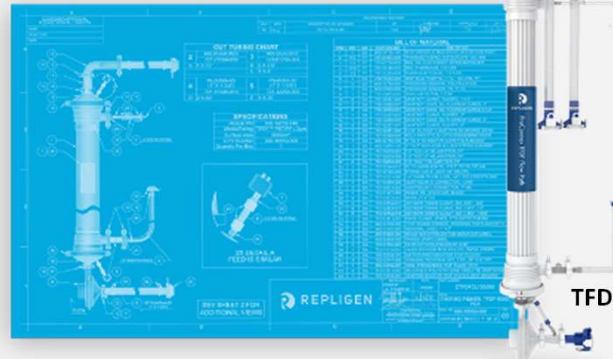
Includes fittings and connections, process reservoirs, pressure transducers, aseptic connectors, TFF filters



Hollow Fiber TFF Flow Paths



Flat Sheet TFF Flow Paths



TFDF® Flow Paths

ProConnex® TFDF® Flow Paths

Complete flow paths for KrosFlo® TFDF® Systems



Optimized for TFDF®

Closed, gamma-irradiated, complete with integrated sensors



Single-use

Ready-to-operate single-use convenience



Integrated

For use with KrosFlo® TFDF® Systems

Flow path surface area

3 cm²

3 cm²

150 cm²

1500 cm²

6000 cm²



Designed-for-purpose rigid consumables and durables

Single-use fluid management



Expertise in non-metallic fabrication and rotational molding

Focus on bioprocessing applications



Custom components meet exact user requirements

- Custom bottles, flasks, carboys, funnels
- Modular totes, carts tanks
- Organizers, clean room equipment



Proprietary valve technology

Single-use fluid management



Expertise in innovative valve technology

- Precision pinch and diaphragm valves with hemispherical plunger geometry
- Proprietary steam to and steam thru designs and sizes
- Basic valves and tubing management



Building blocks of Repligen proprietary flow paths

- Key components of Artesyn® Systems with XO® Technology
- Available as stand-alone components



Designed-for-purpose molded components and extruded tubing

Single-use fluid management



Expertise in molding and extrusion

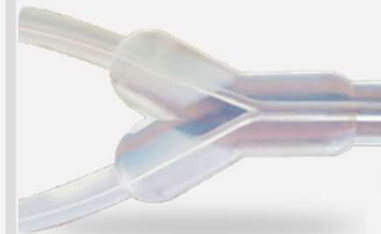
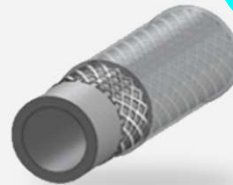
- Molded and over-molded connections
- Eliminated leakage
- Optimum fluid flow dynamics



Custom components meet exact user requirements

- Custom-engineered components
- Connections, bottle stoppers, tube sets with industry-best lead times

Custom -
engineered
components



ELISA Quantitation Kits

Fast, reliable, reproducible ELISA-based protein detection



Best match

Matched standard for

- MabSelect SuRe™ ligand



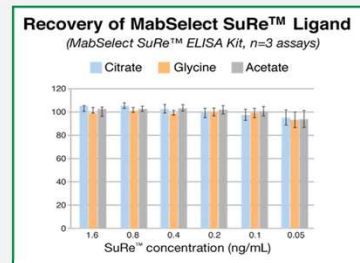
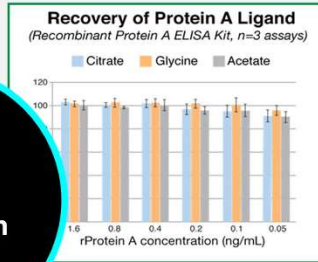
Accurate

Fast, reproducible quantitation of

- MabSelect SuRe™ Ligand
- Native and Recombinant Protein A
- LONG® R3 IGF-I
- NGL-Impact™ A
- NGL COVID-19 Spike Protein Affinity
- NGL-Impact® A HipH



3
sample
preparation
protocols



Captiva® HF Protein A Resin

Protein A resins from the leading manufacturer of rProtein A ligands



Secure supply

- Over 20 years of supply chain trust from the world's leading manufacturer of recombinant Protein A



Reliable performance

- High binding capacity, ≥ 40 mg IgG/mL
- Low Protein A leaching, ≤ 10 ng rSPA per mL



Cost-efficient

- One-third the cost of traditional resins,
- Increased savings when pre-packed into OPUS® columns



LONG[®]R³ IGF-I Cell Culture Supplement

Potent, safe, flexible cell culture growth factor



Better than insulin

200 times more potent and 2 times more stable in cell culture than insulin



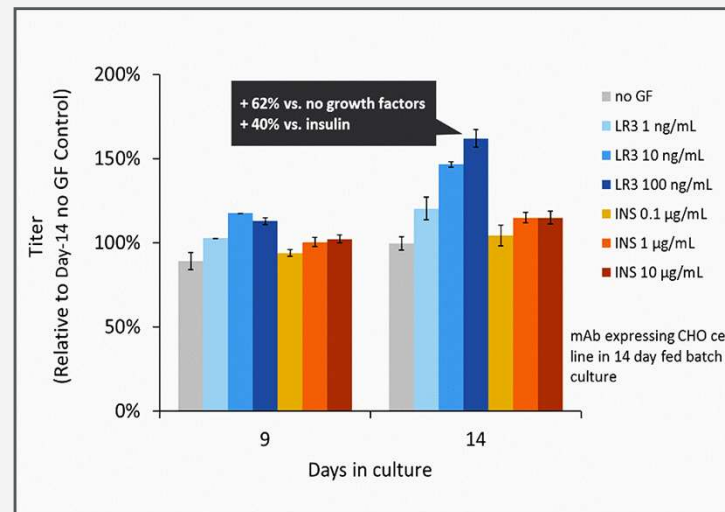
Efficient

Enables more streamlined cell culture feeding strategies with increased cell density, higher viability and extended culture duration



Flexible

Dry or liquid format, use with multiple cell types



6 commercial processes



SoloVPE® Device for Protein Quantitation

The Gold Standard: No Dilution Protein Quantitation



Technology leading method

Compliant, innovative Slope Spectroscopy® method



Fast at-line analytics

No sample preparation or dilution needed



Accurate

- Reduces deviations in manufacturing floor analysis
- Aligns multi-site analytical methods

Standard UV



VPE Spectroscopy

