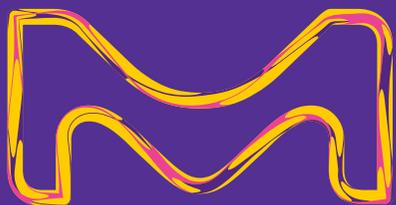
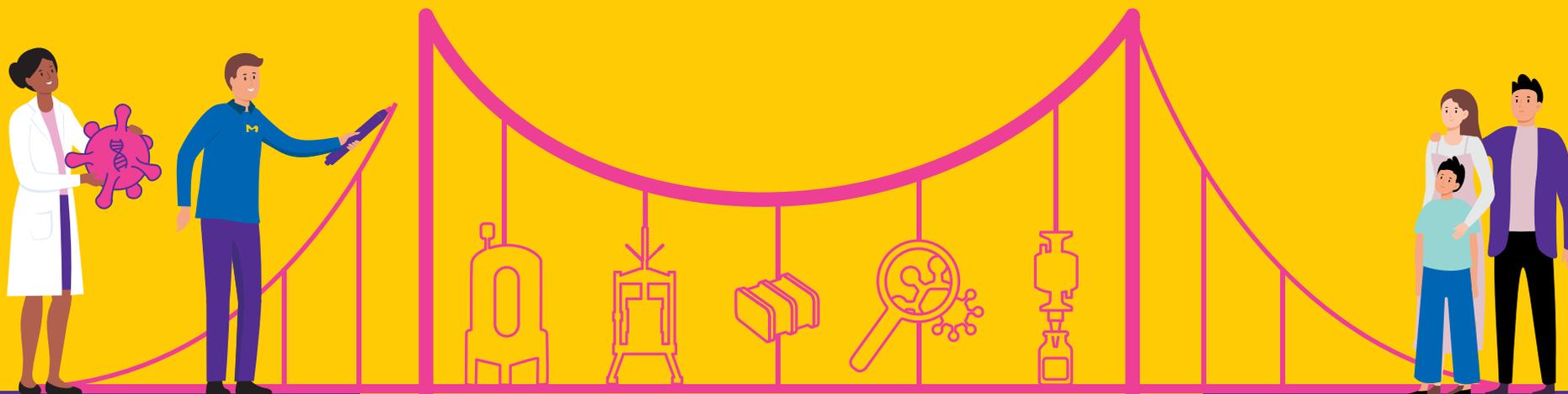


# DRAW ON OUR EXPERIENCE

Gene Therapy Capabilities



The life science business of Merck operates as MilliporeSigma in the U.S. and Canada.

Millipore®

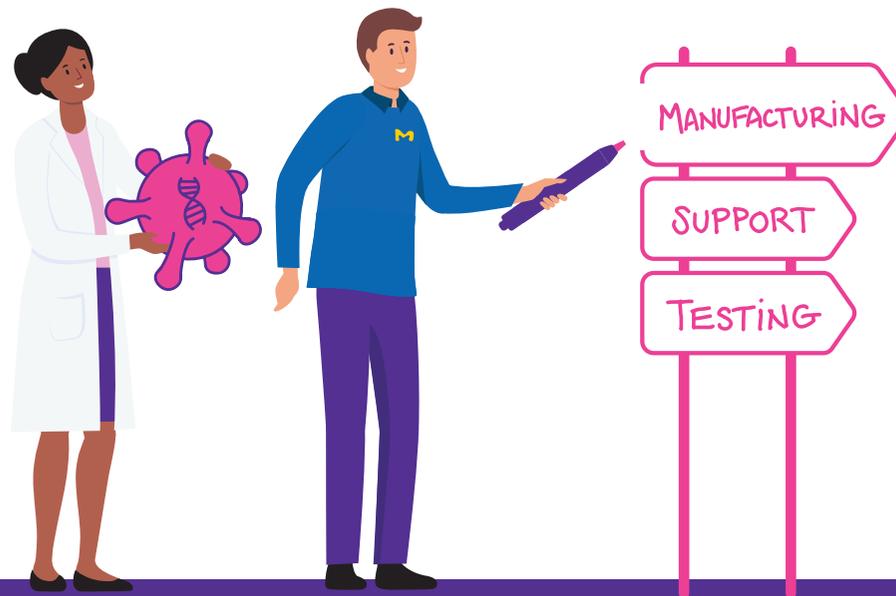
SAFC®

BioReliance®

# Introduction

You've created a gene therapy with the possibility to help patients. But the development and manufacturing of your gene therapy, how it's developed, produced and approved, are still being outlined. No process template exists. You have to design one as you go, despite the uncertainty and unique challenges. We're here to help. With 30+ years of gene therapy experience, we bring expertise in viral vector manufacturing and testing as well as a global organization to integrate process development, scale-up, safety testing and regulatory guidance to meet your process needs.

Our products and services for AAV, Lentivirus and other viral vectors provide solutions to your most challenging pain points around process development, speed, manufacturing and regulatory guidelines. We are ready for you to draw on our experience to help bring your gene therapy to life.



# Our Portfolio of Brands

Merck has brought together the world's leading Life Science brands, so whatever your life science problem, you can benefit from our expert products and services.

## Millipore®

The Millipore® portfolio from Merck offers an ecosystem of industry-leading products and services, spanning preparation, separation, filtration and monitoring – all of which are deeply rooted in quality, reliability and time-tested processes. Our proven products, regulatory and application expertise are a strong foundation you can rely on to consistently perform at the highest level.

## SAFC®

The SAFC® portfolio from Merck offers customized and ready-to-use raw material solutions, backed by deep regulatory expertise. Our high-quality products and services are supported by an experienced and responsive team of raw material and regulatory experts who are committed to understand your requirements and provide tailored solutions that meet your exact needs.

## BioReliance®

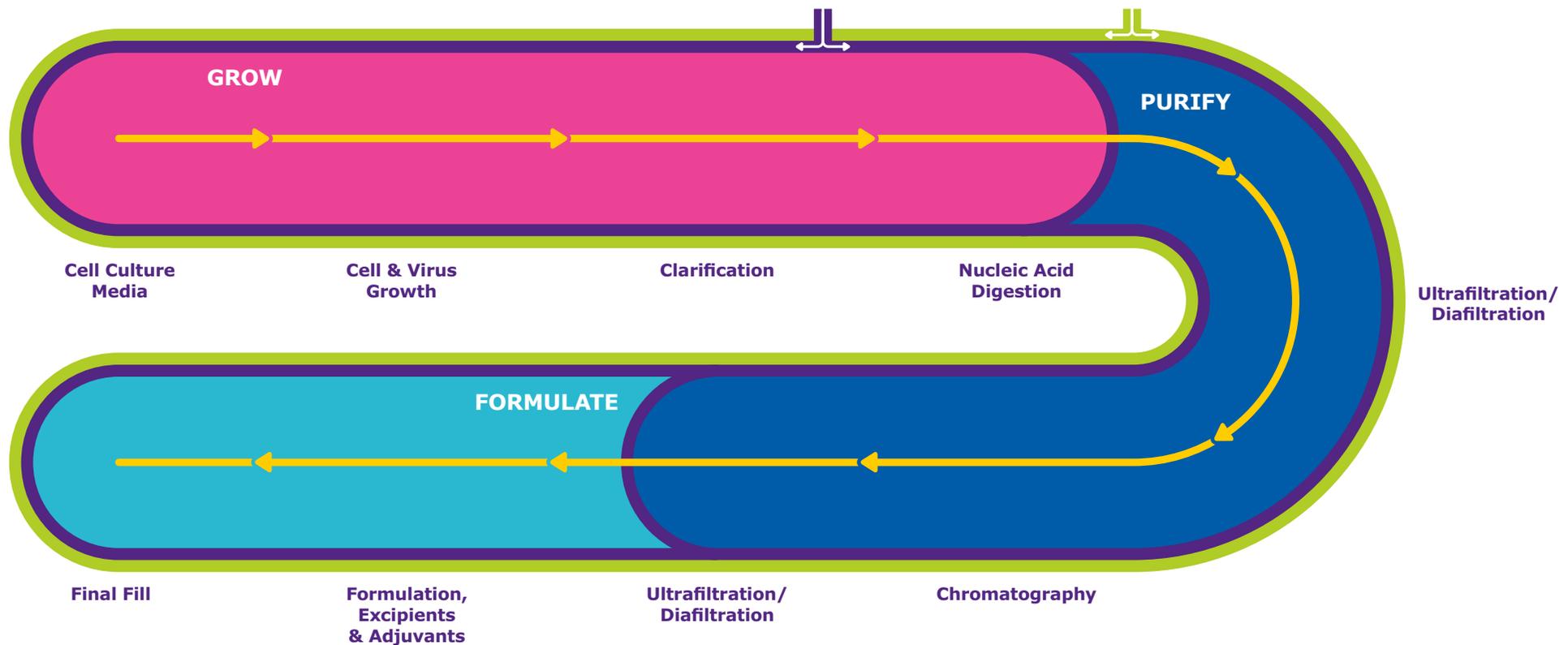
The BioReliance® portfolio from Merck encompasses biopharmaceutical characterization, safety testing and process development, as well as clinical and commercial biomanufacturing. Our experienced teams and operational expertise make us the partner who supports you all the way and always has your vital goal in mind.

# Table of Contents



Our portfolio of products and services can help bring your gene therapy to life.

**Explore our capabilities by clicking on the unit operation below**



# Bioreactors

## Mobius® 3L Single-use Bioreactor

The Mobius® 3L Single-use Bioreactor combines the predictability of a stirred tank design with the flexibility of single use, making it the ideal solution for bench scale cell culture process development.

- Achieve turnaround in a few hours — maximize laboratory resources by saving days of downtime between experiments
- Utilize your existing controller — eliminate the need to purchase additional capital equipment to switch to a single-use solution
- No performance compromise required — comparable functionality to conventional glass bioreactors

# Cell Culture Media

## EX-CELL® CD Insect Cell Medium

EX-CELL® CD insect cell medium, a chemically defined medium that can be used for producing AAV, has been specifically developed for insect cell lines such as the Sf-RVN™\* insect cell line.

- Chemically defined, serum and hydrolysate free — provides high reproducibility and lot-to-lot reliability while reducing the risk of contamination by adventitious agents
- Supports growth and baculovirus infection of Sf-RVN™\* cell line and other insect cells for the production of AAVs, VLPs and recombinant proteins
- Compatible with numerous other insect cell lines such as Sf21, Sf9, Tni, C636 and S2

# Media and Buffer Prep

## Mobius® 2D and 3D Assemblies and Storage Systems

Mobius® 2D and 3D Assemblies and Storage Systems are key components in delivering efficient, scalable and ergonomic process solutions to your production floor.

- Designed to reduce operator error, process risks and improve efficiency
- A full spectrum of systems to choose from, at varying scales and levels of certification that results in greater flexibility, mobility and support for your single-use technologies

# Clarification

## Millistak+® HC Pro Synthetic Depth Filter

Millistak+® HC Pro (High Capacity Synthetic Media) synthetic depth filter provides a cleaner and more consistent depth filtration media over current diatomaceous earth (DE) and cellulose (CE) based filter media.

- Reduces TOC extractables and pre-use flush volume recommendations up to 50%
- Provides as much as two times the filtration capacity with equivalent filter retention properties over commercial DE-based benchmarks
- No beta glucans to interfere with Limulous Amoebocyte Lysate (LAL) testing for bacterial endotoxins

# Nucleic Acid Digestion

## Benzonase® endonuclease Safety Plus Emprove® Expert

Benzonase® endonuclease Safety Plus Emprove® Expert is the smart solution for DNA removal in gene therapy production. Benzonase® endonuclease Safety Plus Emprove® Expert further enhances quality by adding the most recent manufacturing and analytical technologies delivering a higher level of risk mitigation.

- Superior purity  $\geq 99.0\%$  and high activity  $\geq 250$  U/ $\mu$ L
- No protease activity, low bioburden and endotoxins
- Non-Animal-Origin chemically defined fermentation media
- Lot release testing for absence of adventitious viruses and mycoplasma
- Tailgate Sample for large pack sizes
- Emprove® Documentation and U.S. FDA DMF type II file
- Production according to ICH Q7 guideline

# Ultrafiltration/Diafiltration

## Pellicon® 2 Ultrafiltration Cassettes

High-performance tangential flow filters for gene therapy processing including process development, pilot and process scale for concentration and purification applications.

- Leading-edge void-free membranes to match virtually any separation challenge
- Short flow path for higher flux and higher resolution separation capability
- Predictable and fast scale-up
- True linear scalability from laboratory size modules to manufacturing scale assemblies for processing
- Brings higher resolution, improved yields and superior back-pressure resistance

# Chromatography

## Fractogel® EMD IEX Chromatography Resins

Fractogel® EMD ion exchange chromatography resins provide excellent pressure stability resulting in high flow rates and linear scalability. Our proven tentacle technology offers a number of purification advantages compared to conventional resins due to increased accessibility of functional groups and binding of target molecules.

- Reliable purification of macromolecules
- High throughput and selectivity
- Efficient removal of viruses, RNA, DNA, HCP and endotoxins
- Excellent yield and purity
- Superior stability and quality
- Tangible time and cost savings

# Formulation

## Gene Therapy Formulation Excipients

A wide range of high-quality stabilizers, buffers and salts to successfully formulate your gene therapy. Specifically developed for high-risk applications, our buffers, salts and stabilizers are low in bioburden and endotoxins. Supported by our Emprove® program, our excipients have extensive documentation, helping minimize regulatory and quality-associated risks in your manufacturing.

- Elemental impurity information according to ICH Q3D
- Multi-compendial raw materials facilitate the international drug registration procedures
- Paper-free packaging of our excipients to minimize risk



# Final Filtration

## Millipak® Final Fill Filters

Millipak® Final Fill capsule filters are designed for reliable sterile filtration of small volume, high value solutions. These user-friendly filters minimize hold-up volume and have been validated to protect the aseptic flow path during venting, integrity testing and sampling.

- Maximize product recovery in final and high value filtration
- Reduce the risk of microbial and particulate contamination
- Proven Durapore® membrane for high flow rates, low binding and extractables and broad chemical compatibility
- Easy integration into Mobius® single-use final fill assemblies for maximum process flexibility
- Supported by our Emprove® Program: Your fast track through regulatory challenges

# Single-use Flexible Manufacturing

## Mobius® FlexReady Solutions

### Mobius® FlexReady Solution for Tangential Flow Filtration

- Innovative 100% single-use, gamma-irradiated flowpath, combining traditional tubing and film with zero dead legs
- Flexible platform for multi-product and multi-scale production

### Mobius® FlexReady Solution for Chromatography

- Features innovative 100% single-use, gamma-irradiated flowpath and the same instrumentation specifications (pre & post pressure, conductivity, pH and post UV) as our multi-use system
- Single-use flowpaths for maximum process adaptability and reduced cross-contamination risk
- Delivers high accuracy linear and step-gradients

# Single-use Mixing Solutions

## Mobius® Power MIX

The Mobius® Power MIX single-use mixing solution delivers advanced technology for mixing pharmaceutical ingredients from intermediate to final drug products and for the preparation of process solutions, such as buffers and media.

- With strong magnetic coupling, Mobius® Power MIX's powerful and efficient mixing is ideal for mixing liquids, powders and highly viscous solutions in both upstream and downstream applications
- Powerful magnetically coupled impeller designed to efficiently mix the most challenging buffer, media and biopharmaceutical ingredients
- Decreased risk of contamination with closed, zero dead leg, needle-free sampling and single-use pH sensors

# Single-Use Assemblies

## Mobius® MyWay

The Mobius® MyWay portfolio is a three-tiered design and delivery offering to help gene therapy manufacturers implement flexible manufacturing with greater speed and enhanced supply security.

### Mobius® Select

For fast and easy process set up, configure-to-order assemblies from an optimized component library, shipped in only six weeks.

- The perfect balance of off-the-shelf speed and custom flexibility
- Monitored component supply levels for reliable delivery
- Comprehensive documentation for fast and easy implementation
- Emprove® Dossiers available

# Single-Use Sterile Connectors

## Lynx® Sterile Connectors

Reliable and easy-to-use, Lynx® connectors enable risk-free, sterile fluid transfer and are available in a wide range of types, sizes and configurations.

### Lynx® CDR (Connect, Disconnect, Reconnect) Connector

- Eliminates the risk associated with aseptic connection processes
- Validated for up to six sterile connections and disconnections with wet and pressurized flow path

### Lynx® S2S (Sterile to Sterile) Connectors

- Designed to integrate single-use systems
- Gamma and autoclave-compatible

# Sterile Sampling Solutions

## NovaSeptum® GO Sterile Sampling System

From bioreactor to final sterile filtration, the NovaSeptum® GO sampling system allows sampling throughout the manufacturing process. Flexible formats and volumes adapt to your process for robust, reliable monitoring and quality assurance.

- Closed design maximizes security and reduces the risk of cross contamination for consistent, representative samples
- Secure locking mechanism prevents accidental actuation, protecting your valuable product from exposure and ensuring accurate, reproducible results
- No steam sterilization required in between sampling events
- No dead legs

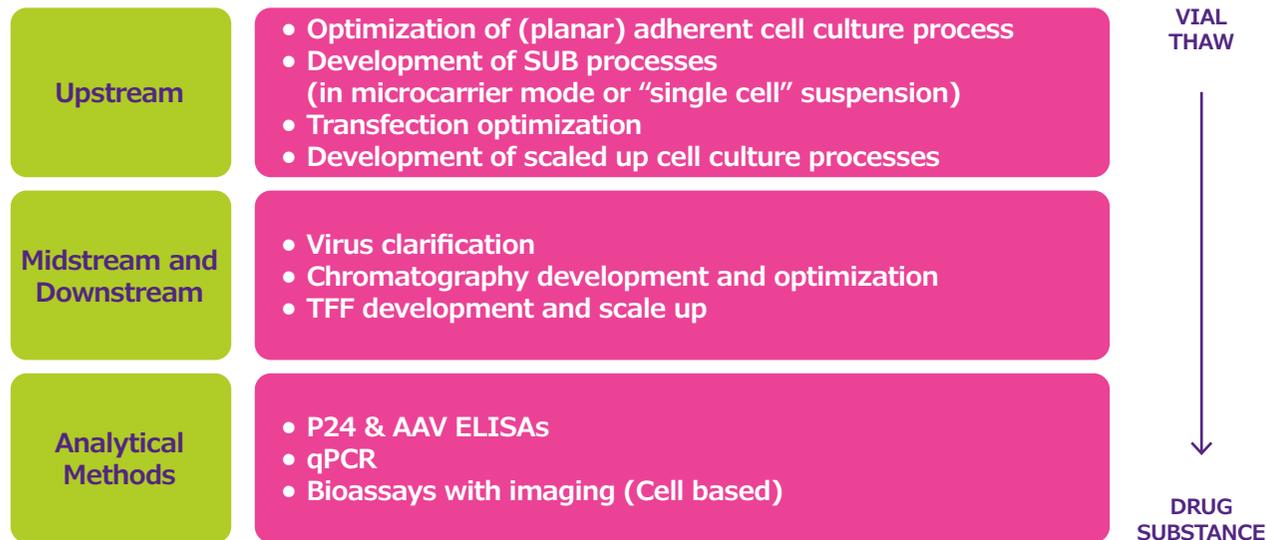
# Viral Vector Contract Manufacturing

## BioReliance® Viral and Gene Therapy Manufacturing

We offer industry-leading quality and experience in cGMP viral vector manufacturing to bring your therapy from development through commercialization.

- Highly qualified process development teams focused on early-stage process optimization all the way through to manufacturing of material to support commercial launch
- State-of-the-art facility that accommodates separate areas for scale-up, process validation, Phase III trials and commercial launch
- Deep regulatory expertise including FDA and EMA inspections to minimize risk

“End-to-End” processing over multiple scales, modalities and vectors



# Biosafety and Characterization

## BioReliance® Testing Services

We offer the widest range of assays to fully characterize and analyze the identity, potency, safety and stability of your viral vector. Benefit from our innovative development programs and platform assays, which provide the optimal balance between speed and customization to give you the confidence to get products to market quickly and safely. Our services include:

- Comprehensive cell bank manufacturing, testing and storage
- Viral bank manufacturing, testing and storage
- A portfolio of gene therapy-specific platform assays and routine testing

### Discover the Advantages



#### Acceleration

Get products to patients quickly and safely



#### Expertise

Our R&D team is continuously innovating to optimize existing assays and establish new platform methods



#### Flexible Approach

Client-specific testing programs to meet your critical development timelines



#### Proven Results

Our assays have been included in regulatory filings with agencies worldwide

# Validation Services

## BioReliance® Services

Accelerate and simplify your path to patients by letting our experts help you choose and conduct the appropriate validation services for your filters, assemblies and single-use systems for gene therapy manufacturing.

### Trust our global services network for:

- Bacterial Retention Testing
- Chemical Compatibility
- Integrity Testing
- Extractables and Leachables Testing
- Patient Safety Evaluation
- Regulatory Consultancy and Custom Study Design



# Global Support

## M Lab™ Collaboration Centers

M Lab™ Collaboration Centers provide a global network of vibrant collaboration spaces where you can explore ideas, learn innovative techniques and work side by side with experts to solve critical process development challenges.

With sites around the world, we can quickly accommodate your evolving needs at a time and a place that works for you. Access the support of our global network of more than 200 scientists, engineers and technicians including process development scientists, biomanufacturing engineers and systems process engineers.

- > 25 years of experience in viral product process development
- Together we have trained more than 10,000 people worldwide. Our network of experts are highly skilled and qualified instructors in every sense, combining technical knowledge with field experience and teaching capabilities.

# Emprove<sup>®</sup> Program

## The Advanced Emprove<sup>®</sup> Program

Our portfolio of more than 400 raw and starting materials, as well as a selection of filters and single-use components, comes with comprehensive and thorough documentation not only covering the latest regulatory requirements, but also anticipating industry expectations not yet covered by regulation.

Three different types of dossiers support you throughout the various stages of your operations:

**Material Qualification Dossier** – Provides information to begin material qualification

**Quality Management Dossier** – Answers questions during risk assessment

**Operational Excellence Dossier** – Supports process optimization

## Comprehensive regulatory information at your fingertips

The Emprove<sup>®</sup> Suite is your online gateway to conveniently access all of our Emprove<sup>®</sup> dossiers on demand. The Emprove<sup>®</sup> Suite is always up-to-date and optimized for any targeted search.



# [SigmaAldrich.com/GeneTherapy](https://SigmaAldrich.com/GeneTherapy)

The life science business of Merck operates as MilliporeSigma in the U.S. and Canada.

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