Thermo Fisher SCIENTIFIC

SOFTGEL TECHNOLOGIES OVERVIEW

- API
- BIOLOGICS
- VIRAL VECTOR SERVICES
- EARLY & LATE PHASE DEVELOPMENT
- CLINICAL TRIAL SOLUTIONS
- LOGISTICS SERVICES
- COMMERCIAL MANUFACTURING

patheon

Innovative softgel technologies that maximize your market potential: Where ideation and expertise come together.

Softgel technologies are becoming an increasingly popular dosage form in both the prescription (Rx) and over-the-counter (OTC) markets. With decades of experience and capabilities spanning development through commercialization, our softgel experts understand what it takes to maximize the potential of your product in either market. From our skilled development scientists to our manufacturing operators, you can count on our team to help your project achieve success through ideation and partnership.

Our scientists are skilled in developing softgel formulations in early development to overcome low solubility challenges, speeding new molecules to clinic. We develop softgel formulations for late stage lifecycle management as well, helping our clients retain market share and maximize product lifetime value. Our development and manufacturing capabilities include production of highly potent drugs, DEA-controlled substances (Schedule I–V and List I) and abuse-deterrent products.

And when existing products need new revenue streams, product and brand managers can tap into our softgel expertise and proprietary technologies for new softgel product options. We offer cost-effective and flexible business models ranging from fee for service, licensing of existing products and co-development of proof of concepts.

Thermo Fisher brings value to pharmaceutical and consumer health care companies through ideation sessions and flexible business models that can:

- Develop product Proof of Concept to confirm market interest
- Provide innovation for product lifecycle management
- Provide solutions for Rx, OTC and tablet to softgel switches
- Enhance bioavailability to obtain quicker onset of action
- Provide formulation options for specific patient populations including pediatrics and geriatrics

Discover the patient benefits of softgels and our diverse technologies that can meet the needs of your molecules and markets.

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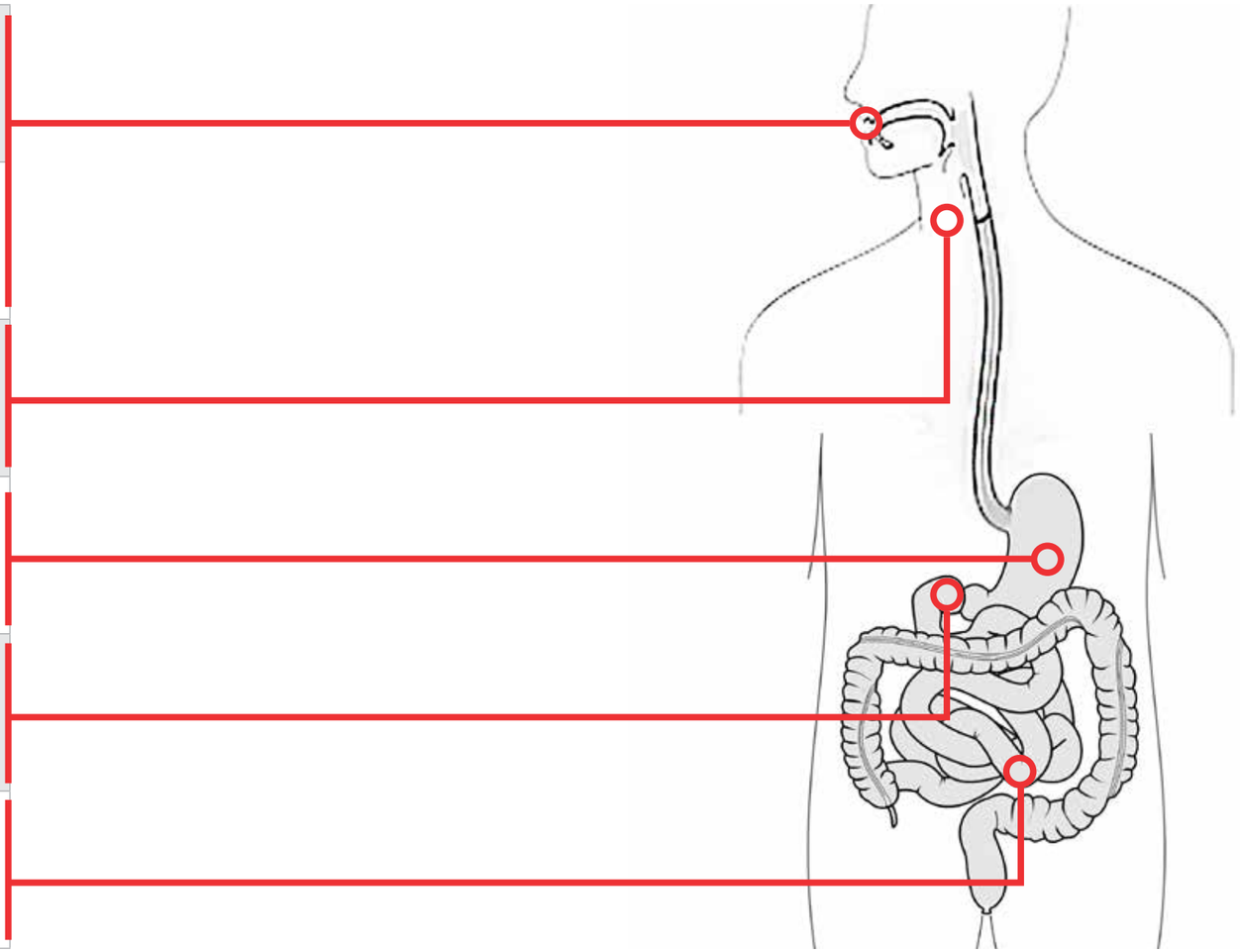
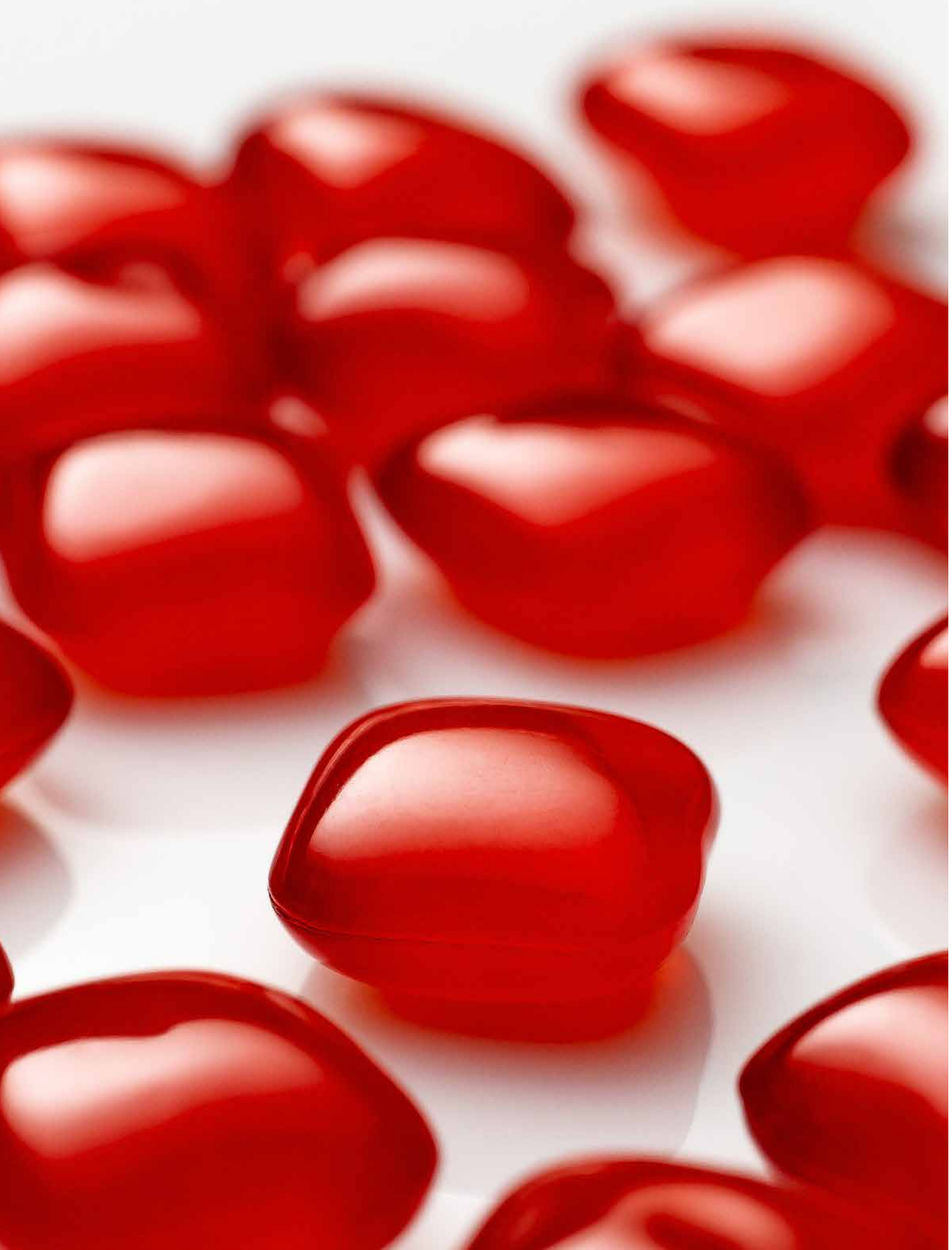
ACTIVATION AREAS

LIQUISOFT™	Chewable Liquid-Filled Softgels
CHEWELS®	Chewable Gels
SOFLET®	Gelcaps
SOFGEL®	Capsules
ENTERICARE®	Enteric Softgels
VERSATROL™	Controlled-Release Softgels





Chewels® chewable gels are approved for pharmaceutical use and are ideal for pediatric and geriatric populations.

They are also well suited for people who find swallowing difficult and are looking for a convenient dosage form for administration. The chewable gels have a soft texture and can be chewed within a minute. No water is needed. The technology provides an opportunity for taste masking, adding another element to patient acceptance and compliance.

Chewels gels are an excellent dosage option for APIs that can be absorbed in the oral cavity, increasing the rate of absorption and circumventing first pass metabolism.

Chewels technology provides a unique opportunity for not only development projects, but also for lifecycle management or pediatric development plans. Clients can augment their current portfolios with a distinguished concept that adds value to their products.

Enteric delivery is critical for the protection of acid-labile compounds from the gastric environment.

It also improves tolerability of APIs that cause gastric irritation, increases bioavailability for certain molecules and provides targeted relief in the small intestine. It can also prevent acid reflux from the medication.

Thermo Fisher Scientific's EnteriCare® technology incorporates the enteric properties directly into the gelatin shell, replacing extra steps such as coating during the manufacturing process. This creates more consistent enteric behavior, as enteric coating is challenging when it comes to capsule homogeneity and long-term stability.

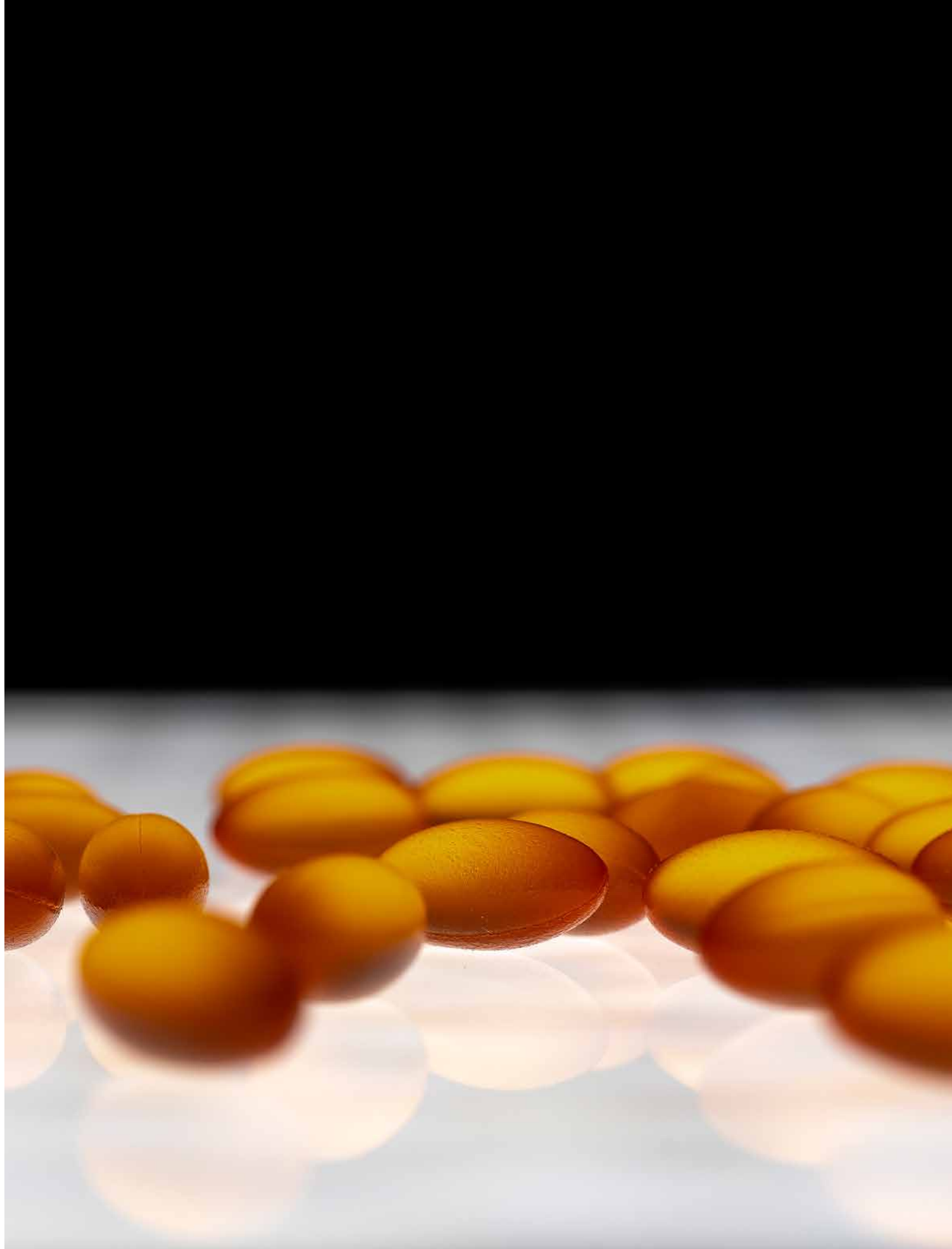
EnteriCare products can be developed as transparent softgels, which creates a more appealing aesthetic quality compared to traditionally coated capsules.

LIQUISOFT™ TECHNOLOGY

With a soft-chewable shell, LiquiSoft™ softgels are particularly suitable for liquid fills that require a fast onset of action and/or buccal absorption.

The technology enhances the performance of poorly soluble compounds and is an accurate, convenient dosage option for oral liquids. LiquiSoft softgels come in a variety of flavors that mask bad tastes and odors, adding to patient appeal.

LiquiSoft softgels feature an optimized polymer shell designed for fast disintegration, as well as flexible fill formulation options to suit APIs with a wide range of physiochemical characteristics. They are formulated to ensure shell-fill compatibility and long shelf life.



SOFGELS® TECHNOLOGY

Sofgels® technology is suitable for liquid formulations, applications requiring faster onset of action, low-dose products and those with poor bioavailability that would benefit from a lipid system. These capsules are easy to swallow, and twist-off options are available.

SOFLET® GELCAPS

Soflet® Gelcaps employ a gelatin-enrobing technology that makes tablets easier to swallow.

Soflet technology is an excellent choice to safely encase highly potent compounds and is particularly suitable for clinical trial blinding. A broad palette of colors and imprinting choices are available, including inline printing.

VERSATROL™ CONTROLLED RELEASE SOFTGELS

Versatrol™ controlled release softgels possess a unique matrix system to fine-tune release and are compatible with lipophilic and hydrophilic formulations.

This technology is suitable for compounds with low solubility, and the controlled release capabilities are integrated into the fill.

Versatrol softgels can be formulated with a customized release profile for the API (it is determined by the penetration rate of the liquid). The dosage form also maintains therapeutic drug level with fewer doses per day, which could increase patient adherence and convenience.

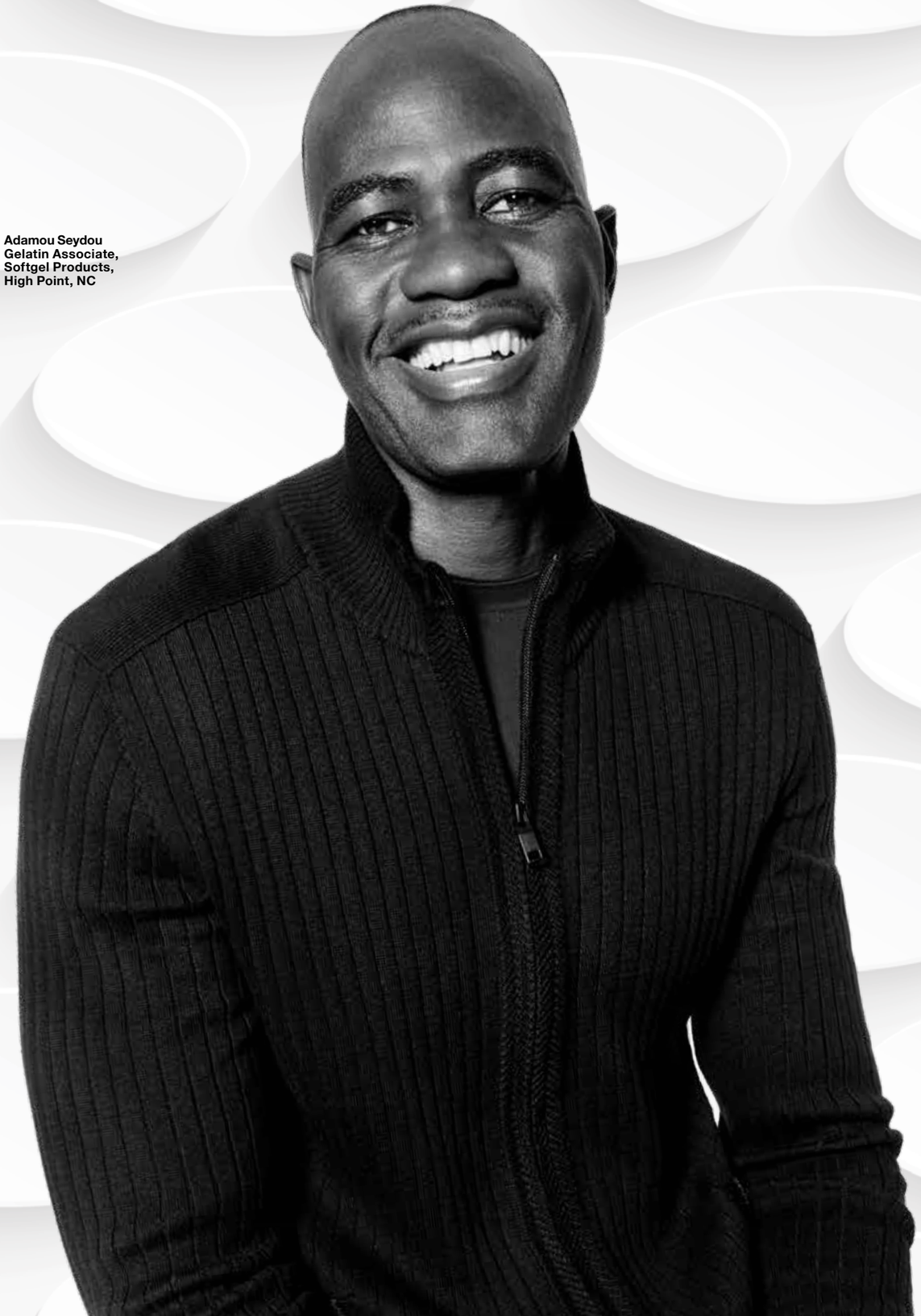
Versatrol softgels have an innovative tamper-resistant technology, making them an excellent choice for abuse-deterrent formulation and/or preventing dose dumping. They are immune to injection, sniffing, crushing or dissolving. The controlled release properties are never compromised.

Twist-offs are an ideal dosage form for accurate dosing of oral liquid, covering a broad dosing range.

This technology can help reduce dosing errors observed with other oral liquid formulation by providing the exact amount of liquid needed in the capsule. Twist-offs are suitable for newborns and young infants and are also well-suited for dermatologic products.

Soft lozenges are a preferred dosing option for patients who have difficulty in swallowing.

Easy to administer to geriatric and pediatric populations and have a pleasant taste. Lozenges extend the drug's time within the oral cavity to elicit a specific effect and do not require water intake for administration. With residence time ranging from a few minutes up to 15 minutes, the required target can be tailored. They can be formulated as sugar-free and are pharmaceutical grade.



Adamou Seydou
Gelatin Associate,
Softgel Products,
High Point, NC

MANUFACTURING SITES AND TECHNICAL OPTIONS

SOFTGELS

Summary of Capabilities

High Point, North Carolina, USA

Facility Facts:

Commercial Workforce: 435

Regulatory Approval (key): US FDA, Health Canada

Potency Capability: Cat 3, including hormones with ability to assess for higher categories

Controlled Drug Schedule Registrations: Manufacturing Registration Schedules I-V, List 1 Researchers Registration Schedules II-V

Contact Info:
4125 Premier Drive
High Point, NC 27265
USA

Tel: 336-812-8700

Unique Offerings:

Commercial manufacturing and development of gelatin-based drug delivery dosage forms.

Specialized Capabilities:

- Development and manufacturing with use of specific proprietary softgel technologies, e.g., Chewels®, LiquiSoft™, Soflet®, Solvatrol™ and EnteriCare®
- Taste masking development for chewable dosage forms
- Manufacturing with use of gelatin from different origins: bovine bone, porcine, and non-animal source for capsules
- Color matching and development for dosage forms
- Formulation development for low solubility compounds and bioavailability enhancement
- Tablet to softgel form change development
- Low dose API product development
- Modified release formulation
- Bioavailability enhancement
- Proof-of-concept product development
- Rx to OTC switches

Life Cycle by Dosage Form

Dosage Forms	Early Development					Late Dev	Commercial Supply	
	Process Development	Analytical Development	Phase I	Phase II	Phase III	Commercial Scale Up	Tech Transfer	Regulatory *
Softgel Capsules	●	●	●	●	●	●	●	
Twist-Off Softgels	●	●	●	●	●	●	●	
EnteriCare® Enteric Softgels	●	●	●	●	●	●	●	
LiquiSoft™ Chewable Softgels	●	●	●	●	●	●	●	
Solvatrol™ Enhanced Solubility Softgels	●	●	●	●	●	●	●	
Soflet® Gelcaps	●	●	●	●	●	●	●	
Chewels® Chewable Gels	●	●	●	●	●	●	●	

* No “on-site” regulatory support but site is able to provide contracted document assistance with Annual Reports.

High Point Key Equipment List

Equipment (Features / Scale)		Softgel Capsules	Twist-Off Softgels	EnteriCare® Enteric Softgels	LiquiSoft™ Chewable Softgels	Solvatrol™ Enhanced Solubility Softgels	Soflet® Gelcaps	Chewels® Chewable Gels
Gel Manufacturing	Gel reactors	●	●	●	●	●	●	●
	Gel receivers 250 / 285 L	●	●	●	●	●	●	●
Fill Manufacturing	Medicine containers 60 L / 200 L / 700 L / 1,500 L	●	●	●	●	●		●
	Process unit (Fryma VME, 20 L, and Ekato SRC, 2,000 L)	●	●	●	●	●		●
	Process unit (Fryma VME, 500 L, dedicated to potents)	●	●	●	●	●		●
	Process unit (Ekato, 500 L, dedicated to hormones)	●	●	●	●	●		●
	High shear dissolving mixers	●	●	●	●	●		●
	Low shear mixers	●	●	●	●	●		●
	Colloid mill	●	●	●	●	●		●
	Deaeration equipment vacuum / spinning disc	●	●	●	●	●		●
Encapsulation	High output encapsulation machines (20 total lines including dedicated potent and hormone lines)	●	●	●	●	●	●	●
	Technophar dryers	●	●	●	●	●	●	●
	Spain dryers	●	●	●	●	●	●	●
	Soflets manufacturing equipment modules						●	
Drying	Drying tunnels (temperature and humidity controlled)	●	●	●	●	●	●	●
Inspection & Bulk Packaging	Polishers	●	●	●	●	●	●	●
	Sizing equipment	●	●	●	●	●	●	●
	Metal detection equipment	●	●	●	●	●	●	●
	Counting equipment	●	●	●	●	●	●	●
	Bulk packaging lines with automated vision inspection	●	●	●	●	●	●	●
	Bulk label printer	●	●	●	●	●	●	●
Printing	High output Ackley ramp feed printer	●	●	●	●	●	●	●
	Ackley VIP	●	●	●	●	●	●	●
Pilot-scale GMP bottling and blister line		●	●	●	●	●	●	●

* For detailed equipment information please contact your Thermo Fisher Scientific representative.

SOFTGELS

Summary of Capabilities

Tilburg, Netherlands

Facility Facts:

Pharmaceutical Development Workforce:	~23
Commercial Workforce:	~180
Regulatory Approval (key):	IGZ (Netherlands, EU - GMP), FDA (USA), ANVISA (Brazil), Saudi Arabia, Belarus
Potency Capability:	Up to Cat 3b
Controlled Drug Schedule Registrations:	None
Contact Info:	De Posthoornstraat 7 5048 AS Tilburg The Netherlands Tel: +31 13 4624 100

Unique Offerings:

Commercial manufacturing and development of gelatin-based drug delivery dosage forms.

Specialized Capabilities:

- Product development expertise from pre-formulation into commercial product for prescription (Rx), over-the-counter (OTC) and nutraceutical dosage forms
- Manufacturing of clinical supplies
- Manufacturing with use of specific proprietary softgel technologies e.g., Chewels®, LiquiSoft™ and EnteriCare®
- Manufacturing with use of gelatin from different origins: bovine bone, porcine, fish
- Color matching and development for dosage form
- Taste masking development for chewable dosage forms
- Formulation & analytical development for low solubility compounds; solubility screening
- Development and small-scale manufacturing of high-potent (Up to class 3B) compounds
- Bioavailability enhancement
- Proof-of-concept product development
- Rx to OTC switches

Life Cycle by Dosage Form

Dosage Forms	Early Development					Late Dev	Commercial Supply	
	Process Development	Analytical Development	Phase I	Phase II	Phase III	Commercial Scale Up	Tech Transfer	Regulatory
Softgel Capsules	●	●	●	●	●	●	●	●
Twist-Off Softgels	●	●	●	●	●	●	●	●
EnteriCare® Enteric Softgels	●	●	●	●	●	●	●	●
LiquiSoft™ Chewable Softgels	●	●	●	●	●	●	●	●
Versatrol™ Controlled Release Softgels	●	●	●	●	●	●	●	●
Solvatrol™ Enhanced Solubility Softgels	●	●	●	●	●	●	●	●
Soflet® Gelcaps	●	●	●	●	●	●	●	●
Chewels® Chewable Gels	●	●	●	●	●	●	●	●

Tilburg Key Equipment List — Commercial / Development Scale

Equipment (Features / Scale)		Softgel Capsules	Twist-Off Softgels	EnteriCare® Enteric Softgels	LiquiSoft™ Chewable Softgels	Versatrol™ Controlled Release Softgels	Solvatrol™ Enhanced Solubility Softgels	Soflet® Gelcaps	Chewels® Chewable Gels
Gel Manufacturing	Gel reactors	●	●	●	●	●	●	●	●
	Gel receivers 250 / 285 L	●	●	●	●	●	●	●	●
	Y-stral gel coloring mixers	●	●	●	●	●	●	●	●
Fill Manufacturing	Medicine containers 1 / 5 / 30 / 285 / 800 / 900 / 1500	●	●	●	●	●	●		●
	Process Unit (Fryma VME 1,000 L)	●	●	●	●	●	●		●
	High shear dissolving mixers	●	●	●	●	●	●		●
	Low shear mixers	●	●	●	●	●	●		●
	Colloid mill	●	●	●	●	●	●		●
	Bead / pearl mill	●	●	●	●	●	●		●
	Stone mill	●	●	●	●	●	●		●
	Deaeration equipment vacuum / spinning disc	●	●	●	●	●	●		●
Encapsulation	High output encapsulation machines	●	●	●	●	●	●	●	●
	Technophar dryers	●	●	●	●	●	●	●	●
	Spain dryers	●	●	●	●	●	●	●	●
	Soflets manufacturing equipment modules							●	
Drying	Drying tunnels (temperature and humidity controlled)	●	●	●	●	●	●	●	●
Inspection & Bulk Packaging	Polishers	●	●	●	●	●	●	●	●
	Sizing equipment	●		●	●	●	●	●	●
	Metal detection equipment	●	●	●	●	●	●	●	●
	Counting equipment	●	●	●	●	●	●	●	●
	Bulk packaging lines	●	●	●	●	●	●	●	●
	Bulk label printer	●	●	●	●	●	●	●	●
Printing	High output Ackley ramp feed printer, off-line printing	●		●	●	●	●	●	●
	In-line printing	●	●	●	●	●	●	●	●

* High-potent containment suit for development and small scale manufacturing
* For detailed equipment information please contact your Thermo Fisher Scientific representative.
* Minimum and maximum batch sizes are not necessarily related to scale; batch size requirements are dependent on the project details

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