

## Oral delivery: from discovery to commercial product





# World Leaders in Liquid Fill Capsules

## Our Company

- Founded in 1989
- Based in United Kingdom
- Experts in formulation, analytical development, clinical & commercial manufacturing
- Specialists in anti-infectives, oncology, GI, & pain management therapies
- Dedicated facilities for high potency and standard products

## Our Clients

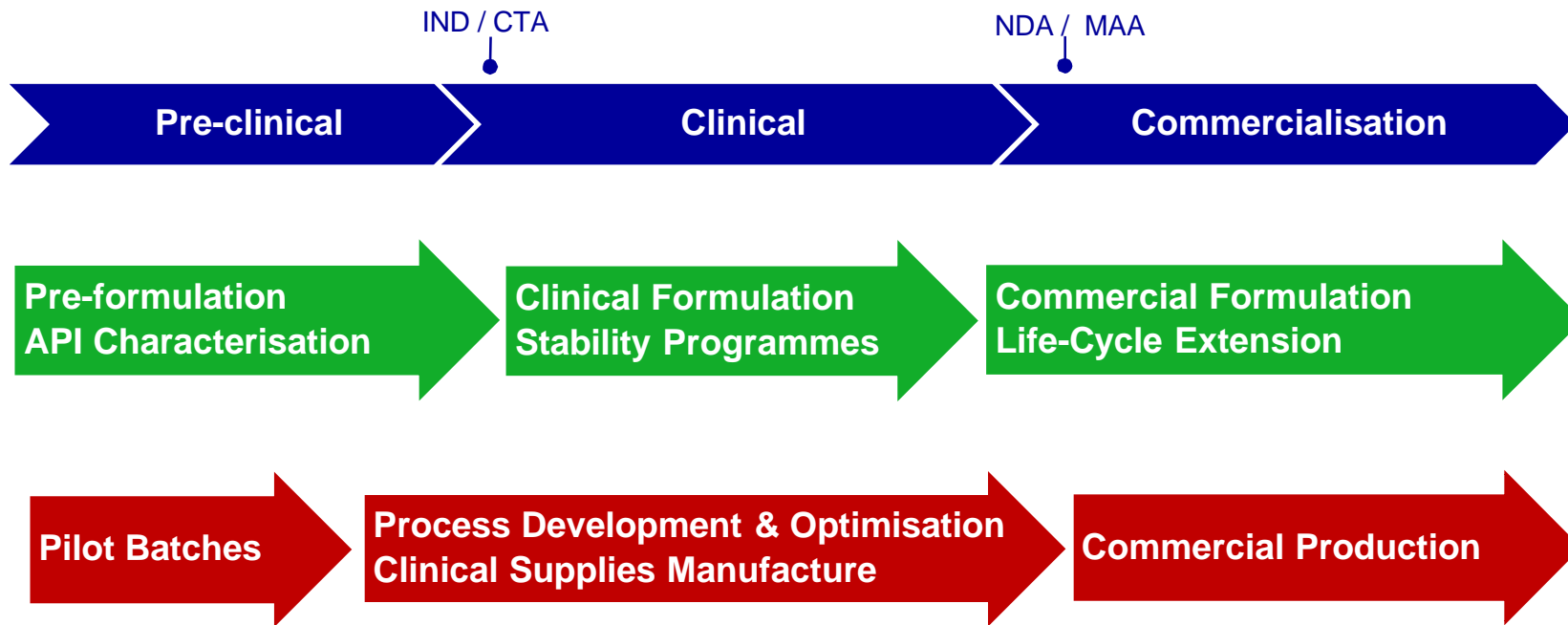
- Over 100 clients in 20 years
- Major pharma, speciality pharma, biotechs, generics, API manufacturers, nutraceutical providers
- Global customer base

## Our Track Record

- MHRA licensed
- FDA approved
- Regular client audits
- > 20 licensed products
- > 2,500 GMP batches manufactured
- Commitment to investment



## One Partner throughout the Product Lifecycle



## Oral Dosage Form Capabilities

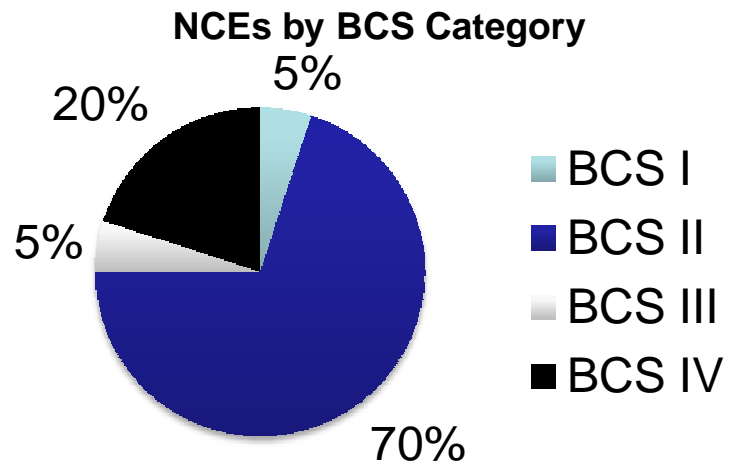
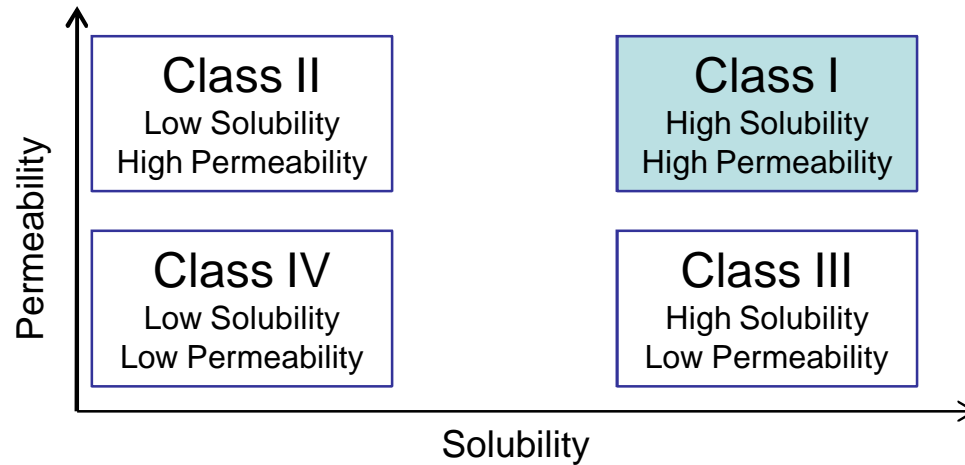
- Liquid Filled Hard Capsules
  - Lipid based formulations
  - Self emulsifying systems (SEDDS)
  - Self micro emulsifying systems (SMEDDS)
  - Solutions
- Semi solid filled capsules
  - Solid solutions
  - Solid dispersions or suspensions
  - Pastes
- Powder filled capsules
- Combination liquid / liquid, liquid / solid capsule products



## Developing your API



## Bioavailability Enhancement



## Enhancing bioavailability using lipids

- Solubility enhancement
  - Drug solubilised in formulation excipients
  - Eliminates dissolution rate limited absorption
  - Formulation performance not dependent on GI for dissolution
  - Reduced food effect
- Inhibition of precipitation on dilution
- Enhancement of lymphatic absorption – reduces first pass metabolism
- Increased absorption through inhibition of P-glycoprotein efflux mechanism



## Lipid Types

Excipients in formulation	Content of formulation (% w/w)				
	Type I <b>OIL</b>	Type II <b>SEDDS</b>	Type IIIA <b>SEDDS</b>	Type IIIB <b>SMEDDS</b>	Type IV <b>OIL-FREE</b>
Oils: tri, di & mono glycerides	100	40-80	40-80	<20	-
Water-insoluble surfactants	-	20-60	-	-	0-20
Water-soluble surfactants	-	-	20-40	20-50	30-80
Hydrophilic cosolvents	-	-	0-40	20-50	0-50
Type of dispersion	Limited or no dispersion	Rapidly dispersing	Rapidly dispersing	Transparent dispersion	Micellar solution
Digestion requirement	Requires digestion	Likely to be digested	Digestion may not be necessary		Limited digestion

***Rapid selection of the right formulation for your molecule***



## Content uniformity - Improving formulation for low dose products

### The Challenge

- Low dose products can often give rise to poor content uniformity
- Tablet and capsule formulations often cannot achieve acceptable CV% for low doses

### The Solution

- liquid filled capsule formulation

***Encap have considerable experience of developing low dose (<1mg) formulations***



## Case Study: Homogeneity Problems with a Powder-Fill Formulation

- Manufacture of 1mg and 7.5mg doses using the client's existing powder-fill formulation was resulting in low assay levels of the API in the final product
- Aim was to develop a novel LFHC formulation to minimise homogeneity problems
- Encap developed a range of novel prototype liquid-fill hard capsule formulations with RSD levels of less than 1.02%



## Improved stability - oxygen and moisture sensitive APIs

### Vancomycin Case Study

#### The Challenge

- Glycopeptide antibiotic
- Oral dosage used to treat *C. difficile* infection
- Hygroscopic API
- Unsuitable for tablet or powder formulation

#### The Solution

- API formulated in high MW PEG matrix
- Improved stability & convenient use
- Taste masked
- Activity retained



## Polymorphism Solutions

### Common Challenges

- Multiple forms
- Low solubility of thermodynamically stable forms
- Unknown polymorph landscape
- Unexpected form changes

### The Solution

- Dissolve your API
- Emulsion
- Suspension / colloid

***Reduced cost, risk and time to market***



## Accelerated Clinical Development

Aimed at minimising time and expenditure to produce IMP for clinic

### Faster into man

- Simple formulations applicable to any API
- Straightforward manufacturing process
- Small CT batches possible
- Provides molecules with absorption challenges the best chance of successful exposure in FIM studies



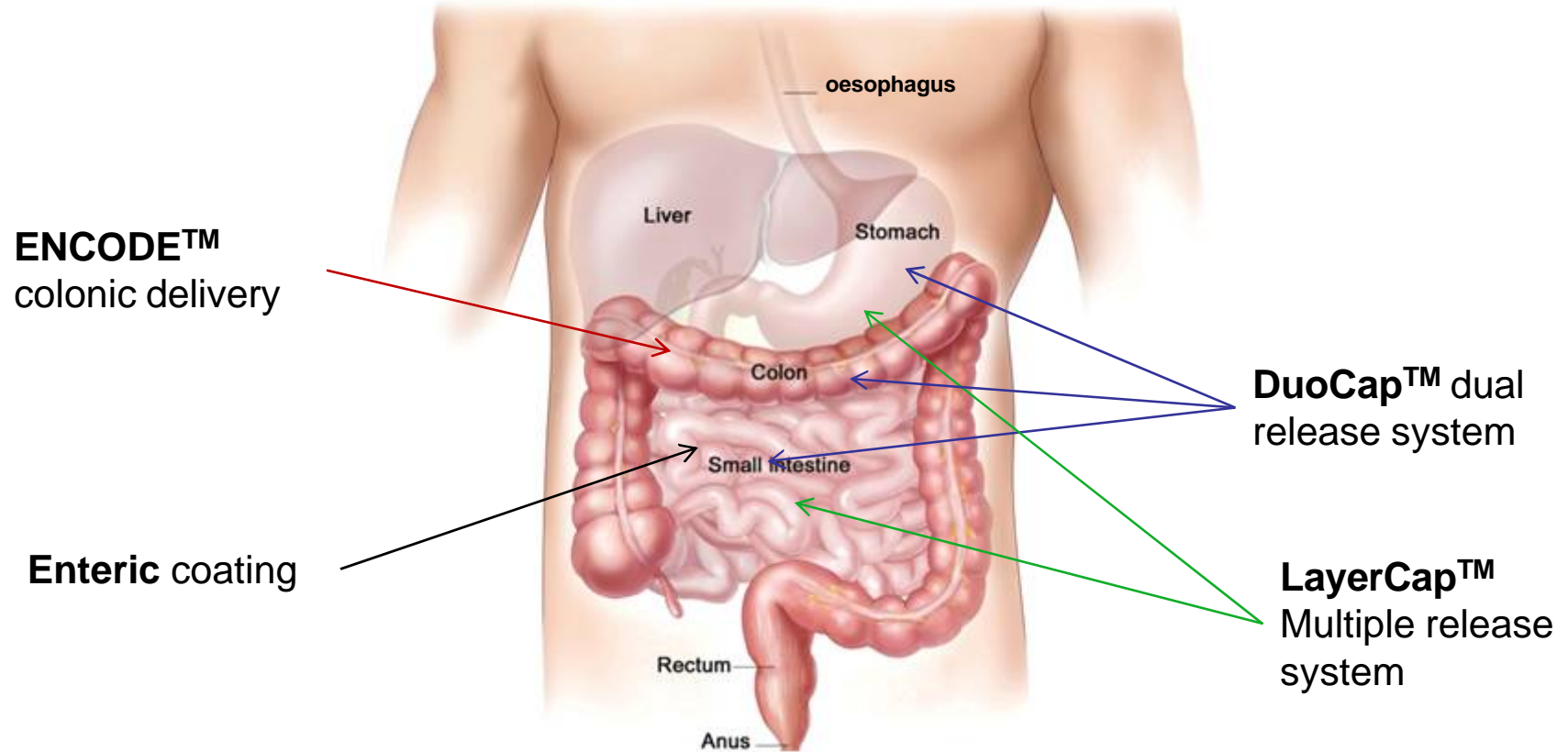
### Accelerates onward Clinical development

- Application of FIM solution to onward development
- Avoid delays due to API physical form issues

***Reduced time and cost to market***

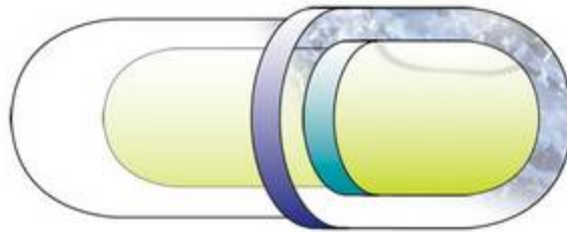


## Targeted delivery

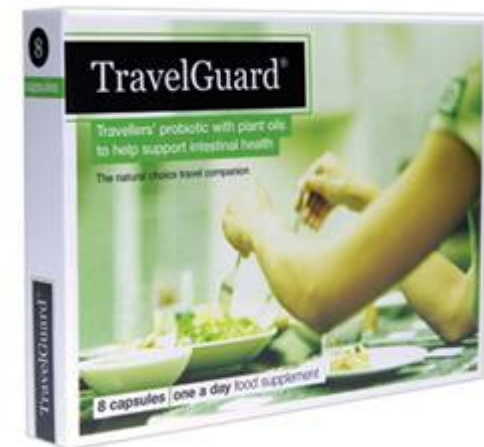


## Targeted delivery – DuoCap

“Capsule-in-a-capsule”



- Two independent compartments in one dosage unit
  - inner capsule contains liquid, semi-solid or powder formulation
  - outer capsule contains liquid or semi-solid formulation
- Delivery targeted to 2 different regions of GI tract
- Sustained, pulsed or delayed release



## Targeted delivery of biomolecules

### The Challenge

- Oral delivery of proteins and peptides
- Domain antibodies
- Oral vaccines

### The Solution

- Formulation designed for optimal biomolecule chemical and conformational stability in part aqueous environment
- Avoid exposure to stomach and targeted delivery to small intestine using enteric coating
- Targeted delivery to colon using ENCODE technologies

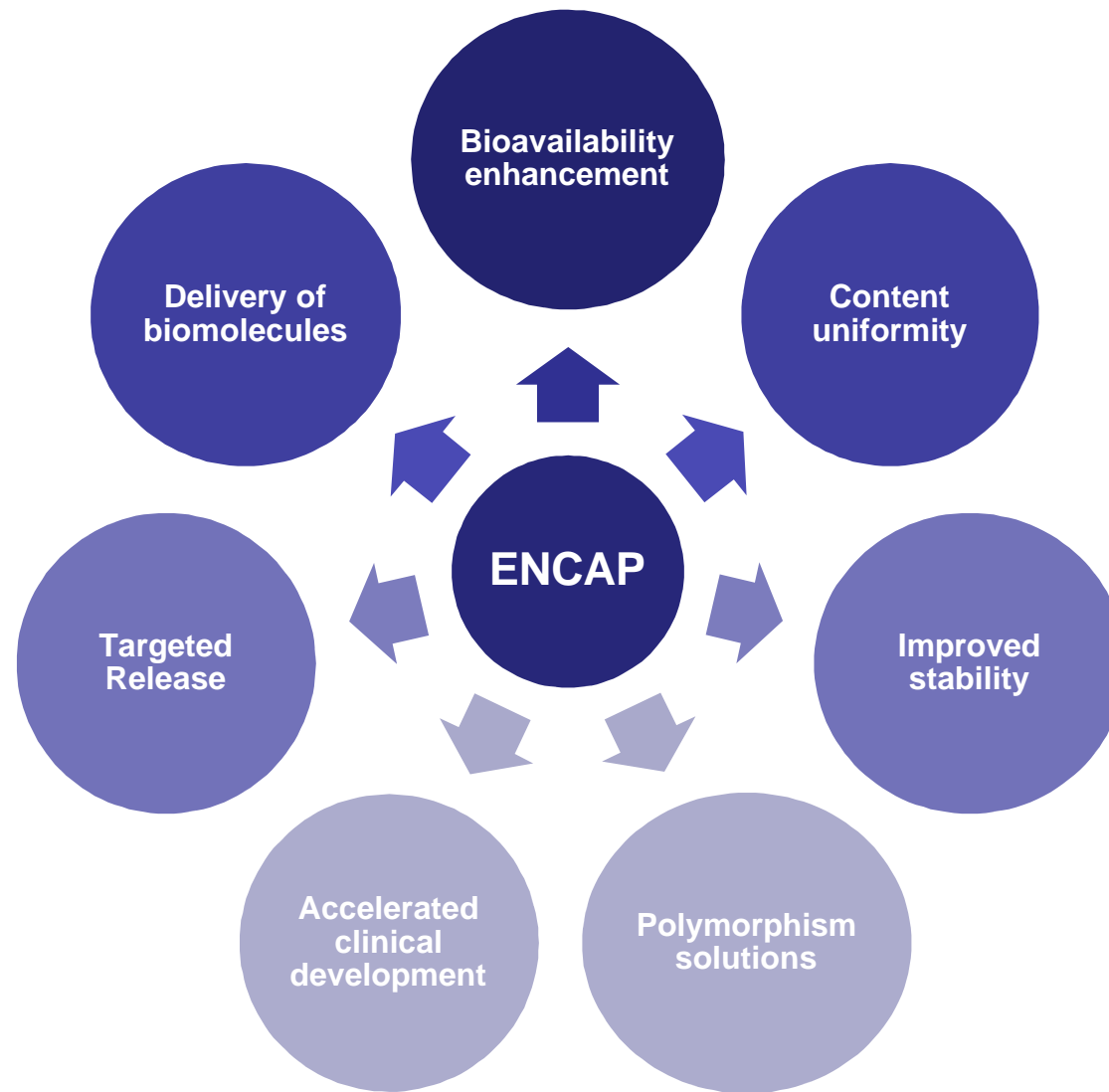


## Coping with diverse APIs & delivery profiles

	Instant release	Sustained release	Multi phase release	Upper GI delivery	Colonic delivery
Hydrophilic small molecules	LFHC	SSFC	DuoCap/ LayerCap	Enteric/ DuoCap	ENCODE
Hydrophobic small molecules	LFHC	SSFC	DuoCap/ Layercap	Enteric/ DuoCap	ENCODE
Peptides / proteins	LFHC	SSFC	DuoCap	Enteric/ DuoCap	ENCODE
Potents	LFHC	SSFC	DuoCap	Enteric/ DuoCap	ENCODE
Controlled Drugs	LFHC	Abusolve	DuoCap/ Abusolve	Abusolve	Abusolve
Combination therapies	DuoCap/ LayerCap	DuoCap/ LayerCap	DuoCap/ LayerCap	DuoCap	ENCODE

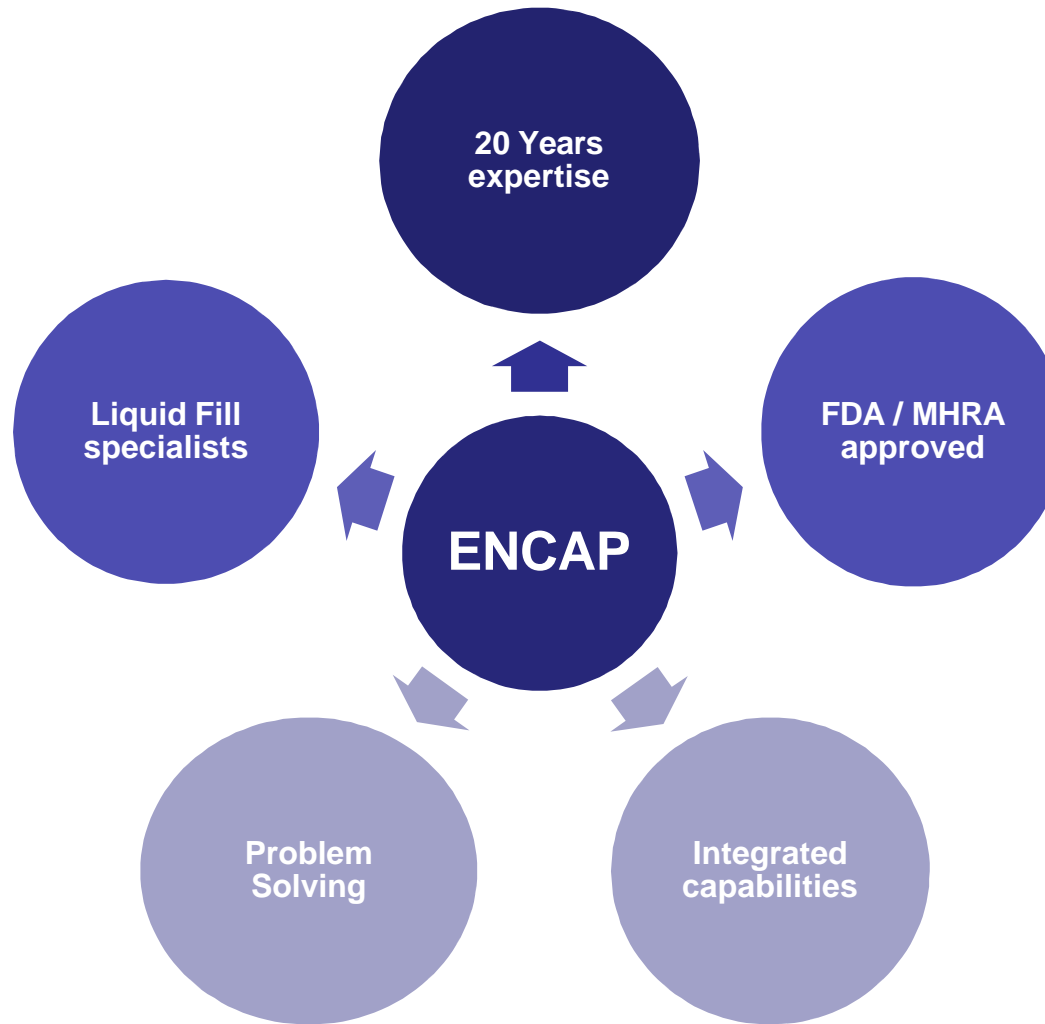
**We have a release modality for *your* molecule**





**Experts in oral drug delivery**

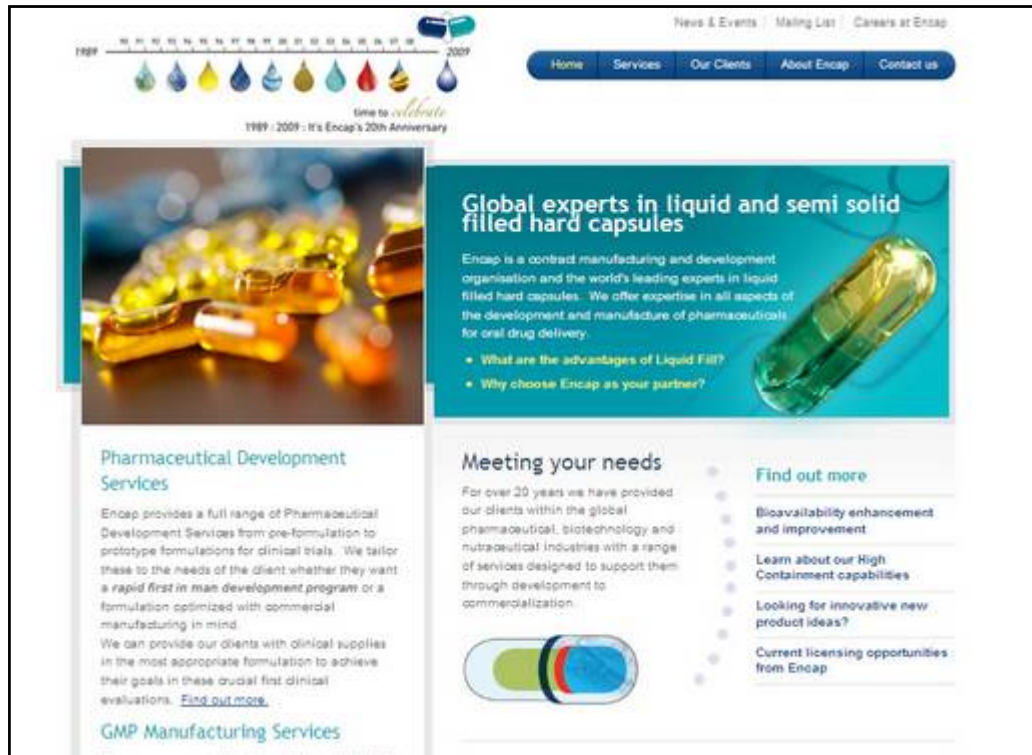




**Our solution will stay with your molecule**



## Want further information?



The screenshot shows the Encap Drug Delivery website. At the top, there is a navigation menu with links for Home, Services, Our Clients, About Encap, and Contact us. Below the navigation, there is a banner for the 20th Anniversary (1989-2009) with a timeline of colored droplets. The main content area features a large image of yellow capsules and a text box titled "Global experts in liquid and semi solid filled hard capsules". The text describes Encap as a contract manufacturing and development organization. Below this, there are three columns of text: "Pharmaceutical Development Services", "Meeting your needs", and "GMP Manufacturing Services". A "Find out more" section is also visible on the right side of the main content area.

### Visit:

[www.encapdrugdelivery.com](http://www.encapdrugdelivery.com)

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