



*The Cyclodextrin Company*



*Getting the best out of Cyclodextrins*

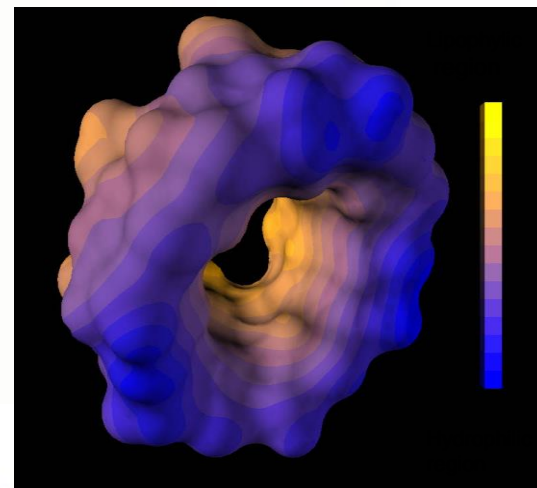
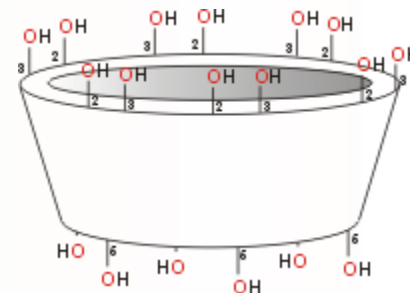
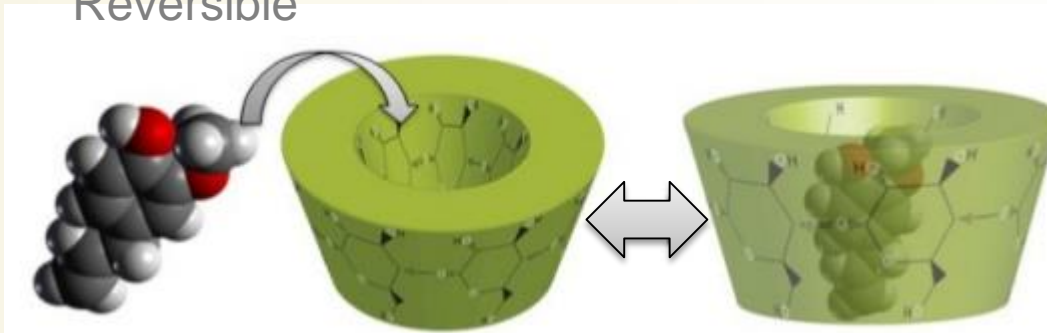
**CYCLOLAB Ltd.**

***Company Introduction  
and Technology Presentation***

# Inclusion complex formation

- Sub-nanometer size cavities  
 $\alpha$ CD 0.57 nm,  $\beta$ CD 0.78 nm,  $\gamma$ CD 0.95 nm
- Primary (bottom) and secondary (top) OH groups are exposed to the solvent
- Hydrophobic cavity / Somewhat hydrophilic outer surface
- Inclusion complex formation with hydrophobic molecules  $\rightarrow$  solubilizing

Non-covalent “host-guest” type interaction  
 Reversible



# Consequences of CD complexation

Cyclodextrins  
may **increase**

***Drug solubility***

***Drug stability***

***Wetting, dissolution rate***

***Absorbed quantity***

Cyclodextrins  
may **decrease**

***Taste***

***Smell***

***Side effect***

***Irritation***

# CDs used in pharmaceuticals

## Oral solution



Itraconazole (Janssen)  
HP- $\beta$ -CD

## Eye drops



Indomethacin  
(Bausch & Lomb)  
HP- $\beta$ -CD



Diclofenac (Novartis)  
HP- $\gamma$ -CD

## Nasal



Estradiol (Servier)  
RM- $\beta$ -CD

## Oral tablets/capsules



Piroxicam (Chiesi)  
 $\beta$ -CD



Ziprasidone (Pfizer)  
SBE- $\beta$ -CD



Cladribine (Merck)  
HP- $\beta$ -CD



Ethinylestradiol/Drospirenon (Bayer)  
 $\beta$ -CD

# CDs used in pharmaceuticals

## Intravenous



Voriconazole (Sandoz)  
SBE- $\beta$ -CD

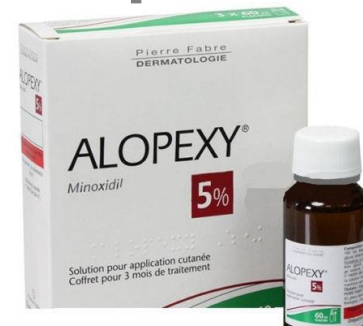


Carfilzomib (Amgen)  
SBE- $\beta$ -CD



Amiodarone (Baxter)  
SBE- $\beta$ -CD

## Topical



Minoxidil (Pierre Fabre)  
 $\gamma$ -CD

## Taste masking



Cetirizine (J&J)  
 $\beta$ -CD



Nicotine (Nicorette)  
 $\beta$ -CD

## Veterinary



Maropitant for dogs  
(Pfizer)  
SBE- $\beta$ -CD



Itraconazole for cats  
(Elanco)  
HP- $\beta$ -CD





The Cyclodextrin Company

# Who are we?

## The world's only **all-round** Cyclodextrin Service Provider

### *Experience*

*CycloLab started as a spin-off of  
Sanofi-Aventis Chinoin Pharma (1989)  
Over 40-year experience in all fields of  
CD-technology*

- over **480** technical/scientific papers
- over **900** technical reports to our customers
- ~ **200** different cyclodextrin derivatives
- ~ **120** patents/applications
- ~ **40** products on the market (5 of them drugs)
- **Drug Master Files** (USA type IV) and **eCTD**
- Over **20,000** citations to CYCLOLAB's papers

### *Expertise & Technology*

*Custom synthesis*

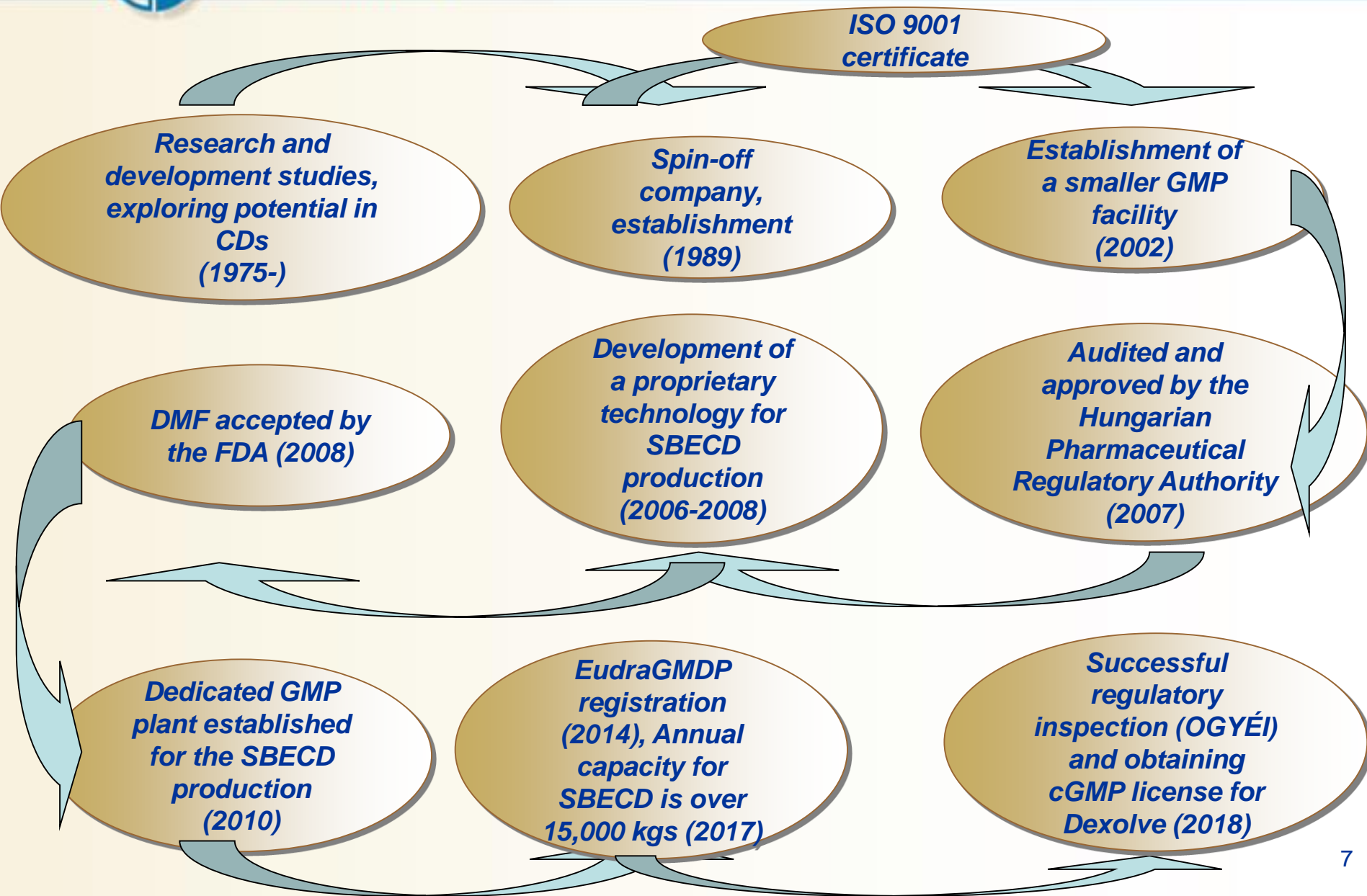
*Drug Solubilization,  
stabilization*

*Other industrial  
applications*

*Cyclodextrin-related  
analytics, stability  
testing*

*GMP-conform  
manufacturing*

# Cyclolab's evolution



# Team and resources

## *Team*

- 16 qualified cyclodextrin scientists
  - 11 PhDs
  - 2 MBAs
  - 2 members in the QA
  - By profession
    - chemists
    - chemical engineers
    - biologists
    - pharmacists
- 12 qualified technicians and operators
- Sales, business dev, logistics, admin

## *Resources*

### 2,000 m<sup>2</sup> (own property) facility

- 2 galenic/technology labs
- 3 analytical labs (GC, HPLC and CZE)
- 2 synthetic chemistry labs
- 150 m<sup>2</sup> cGMP compliant clean room
- 350 m<sup>2</sup> cGMP compliant production area (Spray-drying unit)
- Freeze-drying units

### Quality systems

**ISO 9001:2015**

**cGMP (OGYÉI/57792-7/2018)**

**US FDA DMF Type IV**



# Cyclolab's Portfolio

## GMP Manufacturing

Betadex Sulfobutyl  
Ether Sodium

**DEXOLVE™**

Custom cGMP synthesis  
of CDs,  
CD complexes,  
investigational  
medicinal products

Preparation/filing of  
regulatory dossier

## Products

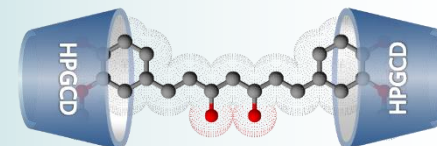
Pharma grade  
CDs

Standard grade  
CDs

Fine chemical  
grade CDs

Single isomer CDs

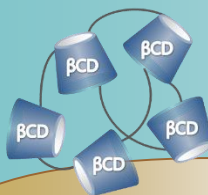
Fluorescent  
derivatives



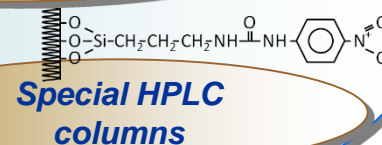
Maltooligomers

CD complexes

Analytical standards –  
Sugammadex impurities



CD polymers



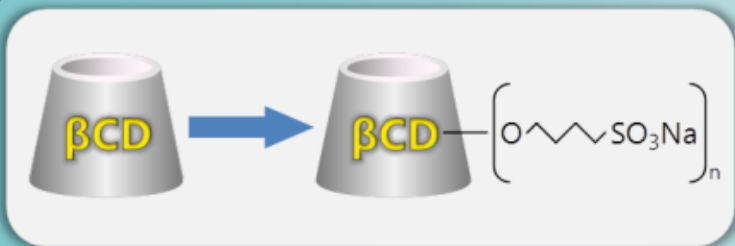
Special HPLC  
columns



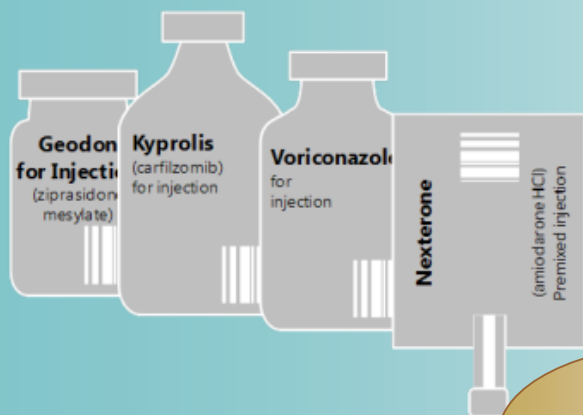
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# Cyclolab's Portfolio

Dexolve™



**EudraGMDP**



**cGMP  
>100 kg/batch  
USP N.F.**

**cGMP certified  
OGYÉI/57792-  
7/2018**

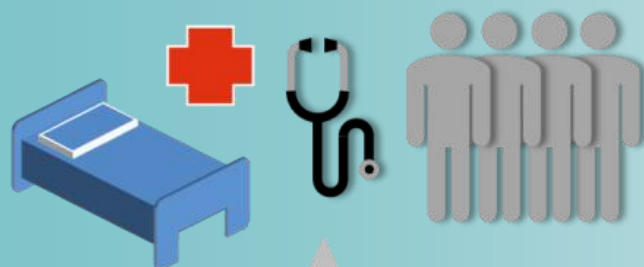
**36 months  
stability  
data**

**>200 batches  
manufactured**

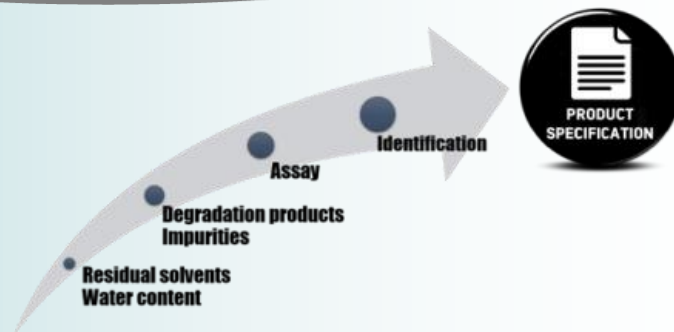
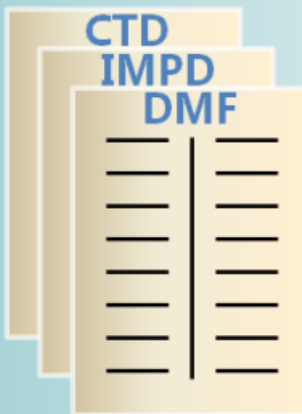
**Annual  
capacity  
over 15,000  
kgs**

**No down payment, no royalty,  
no milestone payment!**

## GMP Synthesis



*Regulatory license for  
manufacture of APIs and clinical  
investigational products*



## Related services – R&D

### Early phase drug development

Customization of CD enabled formulations;  
Investigation of changes in physico-chemical properties;  
Life cycle management

### In vitro bioequivalence studies

Design and performance of in vitro studies to support bioequivalence of a CD enabled formulation.

### Custom cyclodextrin synthesis

Exclusive manufacture, unique synthetic routes, self-tailored products and characteristics

### CD-guest interaction studies

### Analytical services

### Assay, impurity tests

Method development, validation; cGMP release testing of pharma grade CDs; HPLC, GC, CE, UV, MS, NMR, IR, Micro and BET content methods;  
Stability studies

### CD-based chiral separations

### Bioanalytical investigations

## IP services and consultation

Over  
62.000  
CD  
related  
papers

30 years of experience in compilation of CD related patents (synthesis, application, etc), patent claim analysis, consultancy in CD related projects

## Pipeline

### Sugammadex

*Our main efforts are driven into technical and analytical support for companies developing generic Bridion and supply of a wide variety of process impurities*

### NCE Cyclodextrins

*Developing CDs as actives for diseases such as cancer, cardiovascular diseases, neurodegenerative illnesses or as life-saving antidotes*

### Selective drug delivery systems

*Attaching targeting moieties to CDs to develop selective DDSs for cancer therapies*

### Formulation development

*Cyclolab is actively developing formulations to improve performance of known compounds in the pharma and other industries*

### CDs as new class of antibiotics

*A family of CD molecules that may prevent Quorum sensing of bacteria in combination products and as single APIs*

### CDs in biological formulations

*CDs to be applied as artificial chaperones in mAb and other protein formulations to control folding and prevent aggregation, improve stability, replacing detergents*



