

# DBcaps®

**Double blind. Zero bias.**

Stephen Rode / Julien Lamps

26th of May, 2020



# Your presenters today



Julien Lamps,  
Product Manager



Stephen Rode,  
Business Development Manager



---

# Clinical Trials dynamics

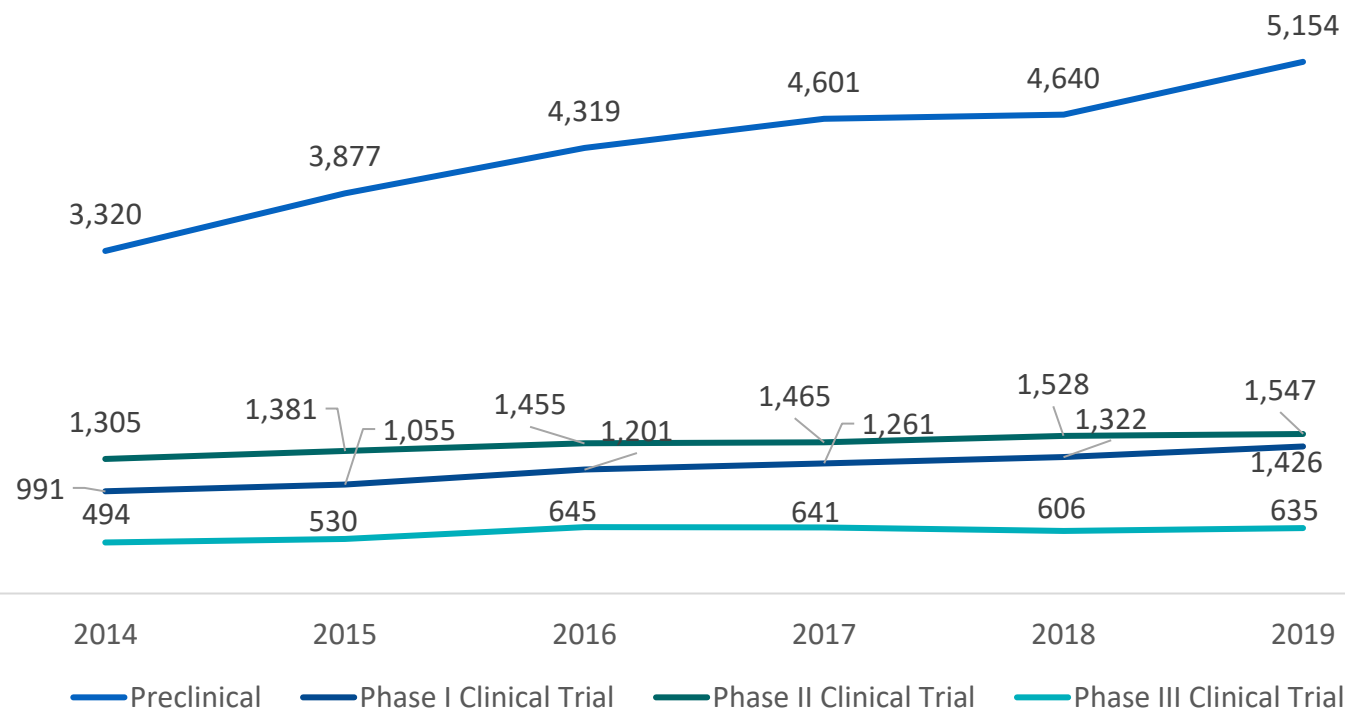
# Development Pipeline Small Molecules

Pipeline 2019

**8762 Drugs**

Pipeline Small Molecule

Phase	CAGR% 2015-19
Preclinical	7.4%
Phase I	7.8%
Phase II	2.9%
Phase III	4.6%

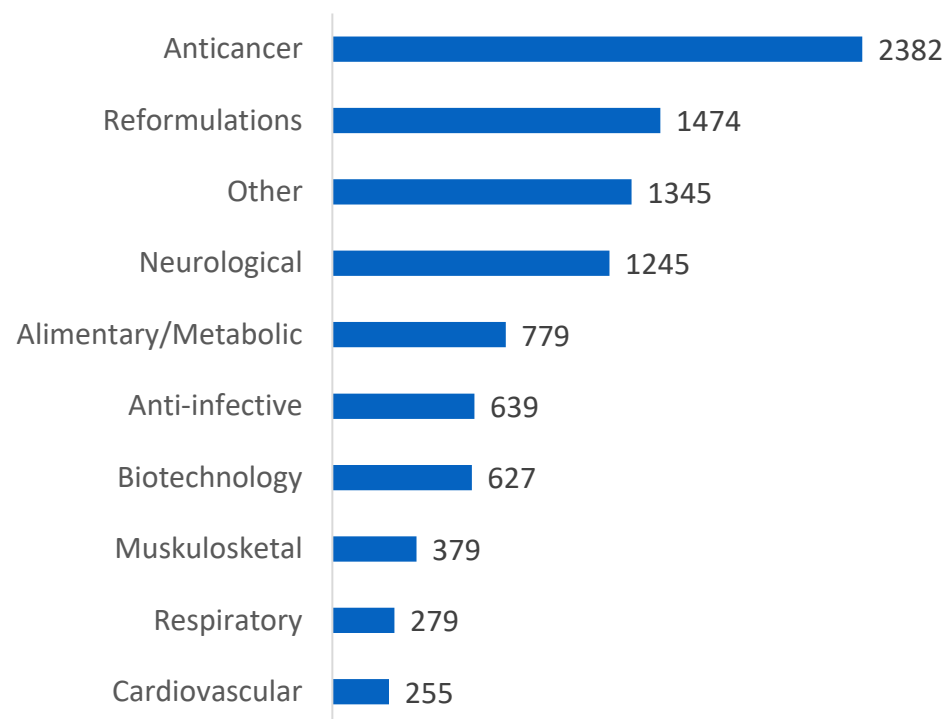


- The total 2019 small molecule Pipeline is **8762 drugs**.
- **Preclinical & Phase I** Pipeline covers **6580 drugs** for Small Molecules, ie **75%** of the whole pipeline.
- Phase I CAGR is **7.8%** for the last 5 years, **105 new** drugs created in this Phase I since 2015.
- The **CAGR** from 2015 to 2019 is **6.4%** for the development Pipeline, with a steady growth for all Phases.

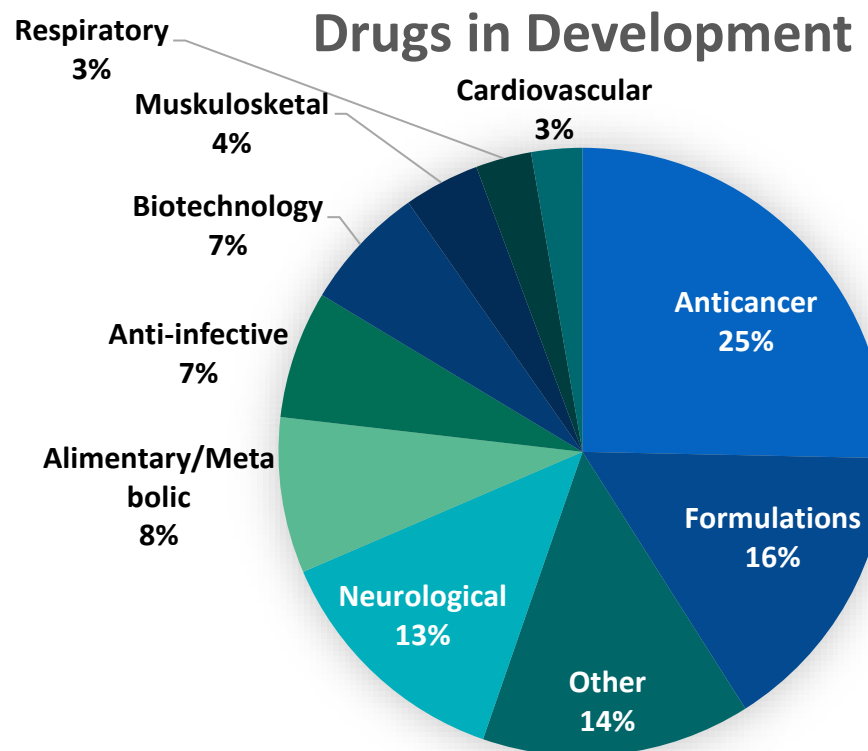
Source: Pharmaprojects® | Informa, 2020

# Small Molecules by Therapeutic Area

Drugs by Therapeutic Area



Drugs in Development

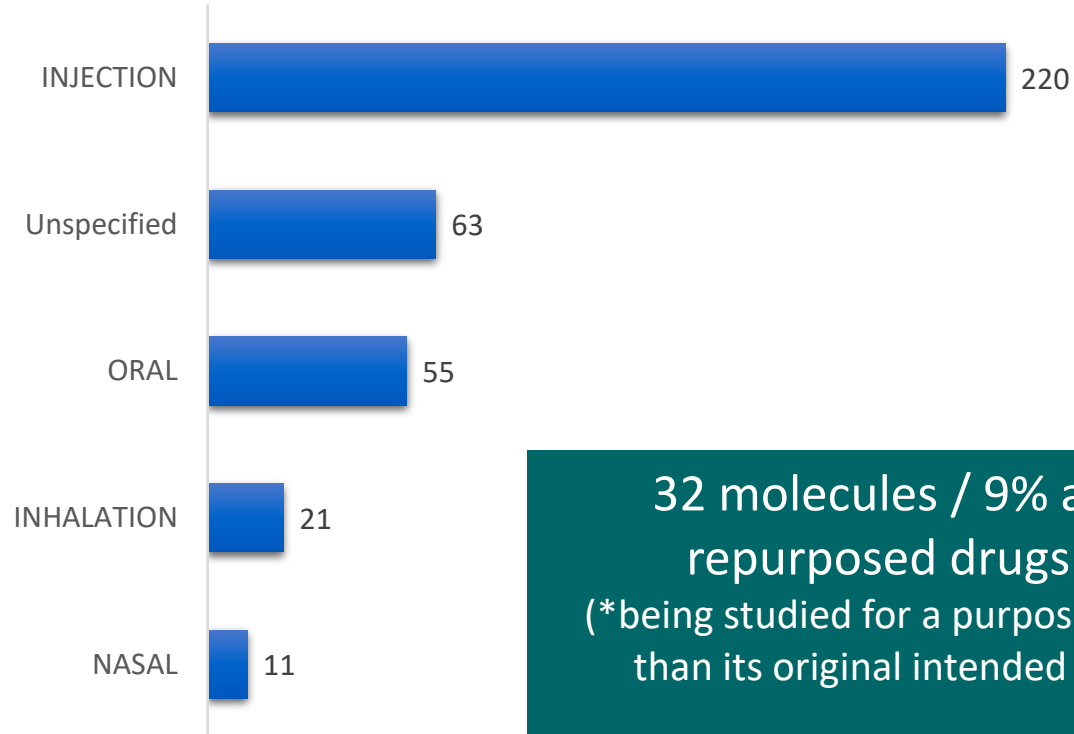


Source: Pharmaprojects® | Informa, 2020



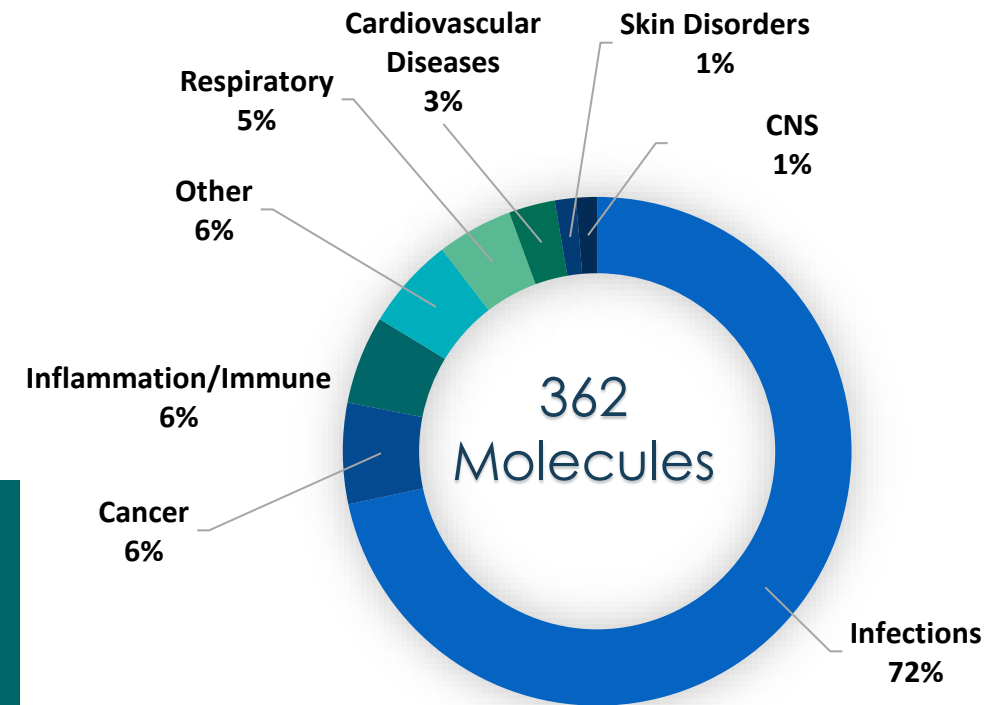
# Covid-19 Pipeline – April, 2020

## Molecules based on Route of Administration



32 molecules / 9% are repurposed drugs\*  
(\*being studied for a purpose other than its original intended use)

## Molecules by Therapeutic Area



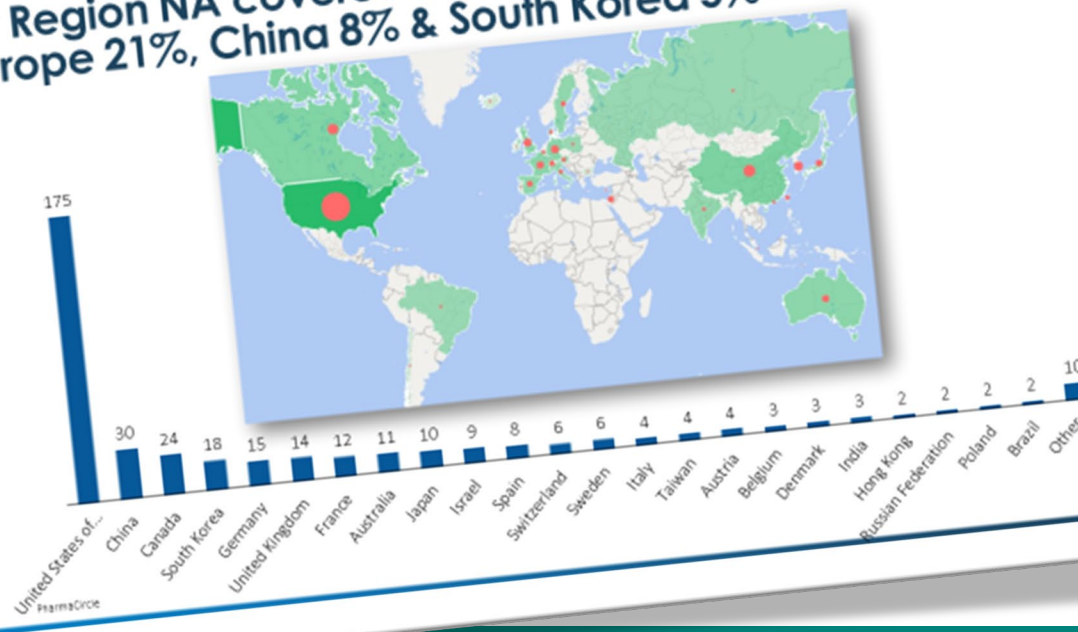
Source : PharmaCircle® – April 2020

# Covid-19

## Molecules in Trials due to June 30, 2020

Antivirals	Immune Boosters	Anti Inflammatories	Mucolytics	Anticoagulants	Vasodilators	Antiogenesis	Antimalarials	Others
<ul style="list-style-type: none"> <li>Arbidol umifenovir</li> <li>ASCO9</li> <li>Azvudine</li> <li>Danoprevir</li> <li>DAS181</li> <li>Emtricitabine</li> <li>Favipiravir</li> <li>Lopinavir</li> <li>Oseltamivir</li> <li>Ritonavir</li> <li>Remdesivir</li> <li>Tenofovir</li> <li>Triazavarin</li> <li>Xiyanping</li> </ul>	<ul style="list-style-type: none"> <li>Arbidol umifenovi</li> <li>Bevacizumab biosimilar</li> <li>Interferon a</li> <li>Interferon a1b</li> <li>Interferon a2b</li> <li>IVIG</li> <li>Nivolumab</li> <li>Novaferon</li> <li>Peginterferon a2b</li> <li>Pembrisizumab</li> <li>Thymosin a1</li> </ul>	<ul style="list-style-type: none"> <li>Adalimumab</li> <li>Alvesco ciclesonide</li> <li>Baricitinib</li> <li>Colchine</li> <li>Leflunomide</li> <li>Methylprednisolone</li> <li>Mesenchymal stem cells</li> <li>MSCs</li> <li>MSC derived exosomes</li> <li>Piclidenoson</li> <li>Ruxolitinib</li> <li>Siltuximab</li> <li>Thalidomide</li> <li>Tocilizumab</li> <li>Tofacitinib</li> <li>Ulinastatin</li> <li>Xiyanping</li> </ul>	<ul style="list-style-type: none"> <li>Bromhexine</li> <li>Ebastine</li> </ul>	<ul style="list-style-type: none"> <li>Heparin</li> <li>Heparin(LMW)</li> </ul>	<ul style="list-style-type: none"> <li>Angiotensin 1-7</li> <li>Dipyridamole</li> </ul>	<ul style="list-style-type: none"> <li>Bevacizumab</li> <li>Thalidomide</li> </ul>	<ul style="list-style-type: none"> <li>Chloroquine</li> <li>Hydroxychloroquine</li> </ul>	<ul style="list-style-type: none"> <li>Lipoic acid</li> <li>Azithromycin</li> <li>Formoterol</li> <li>Levamisole</li> </ul>

By Region NA covered 55% of the Pipeline,  
Europe 21%, China 8% & South Korea 5%



Sources : Biocentury® - April 2020,  
Pharmaprojects® | Informa, 2020

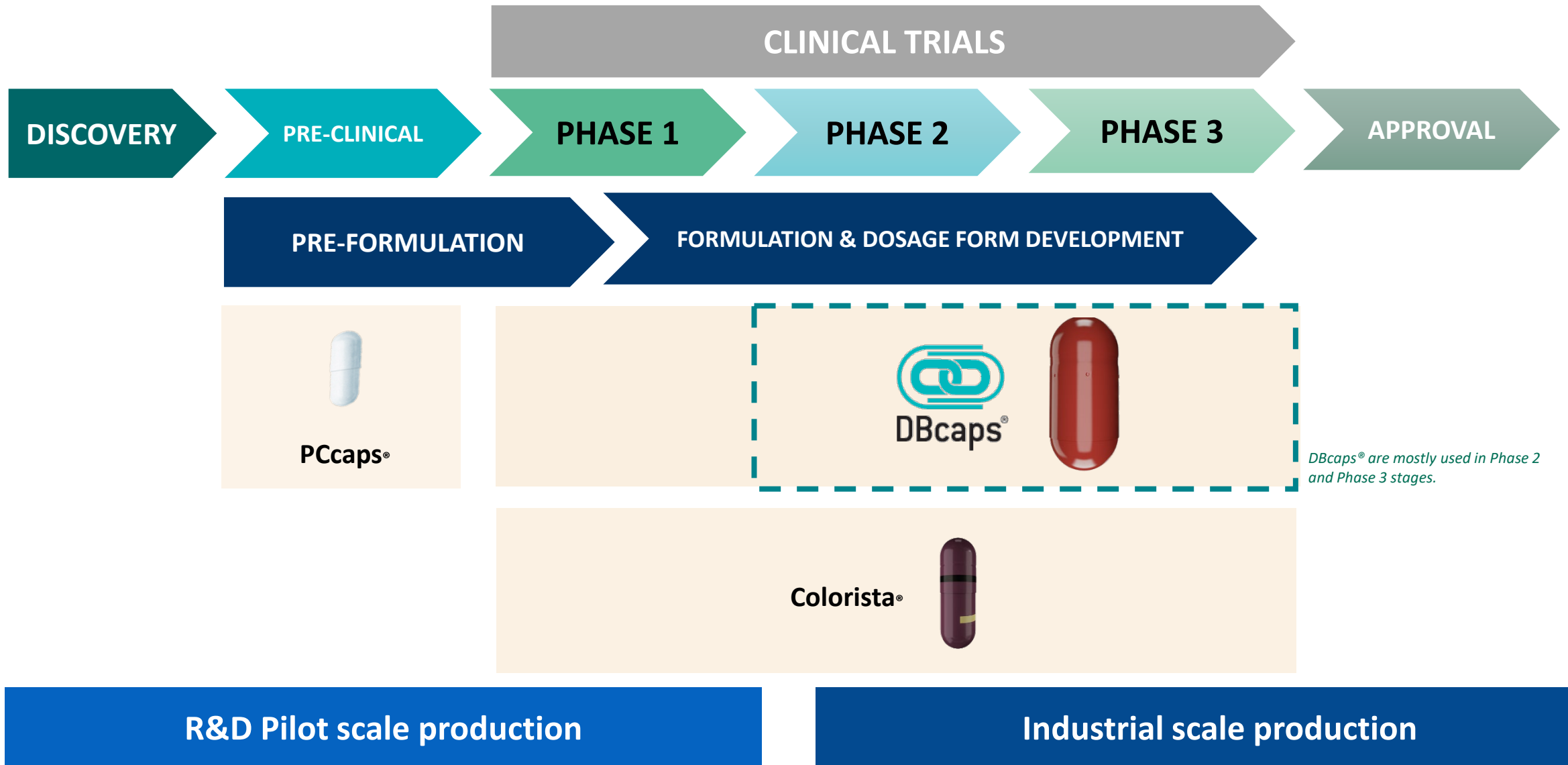
---

# Our DBcaps®





# Capsugel® Pre-Clinical and Clinical portfolio



# A Closer Look at DBcaps® Design



Dual Locking Ring

Extended Cap Length

Double layer of opaque material

# Features & Benefits



## OUR OFFER

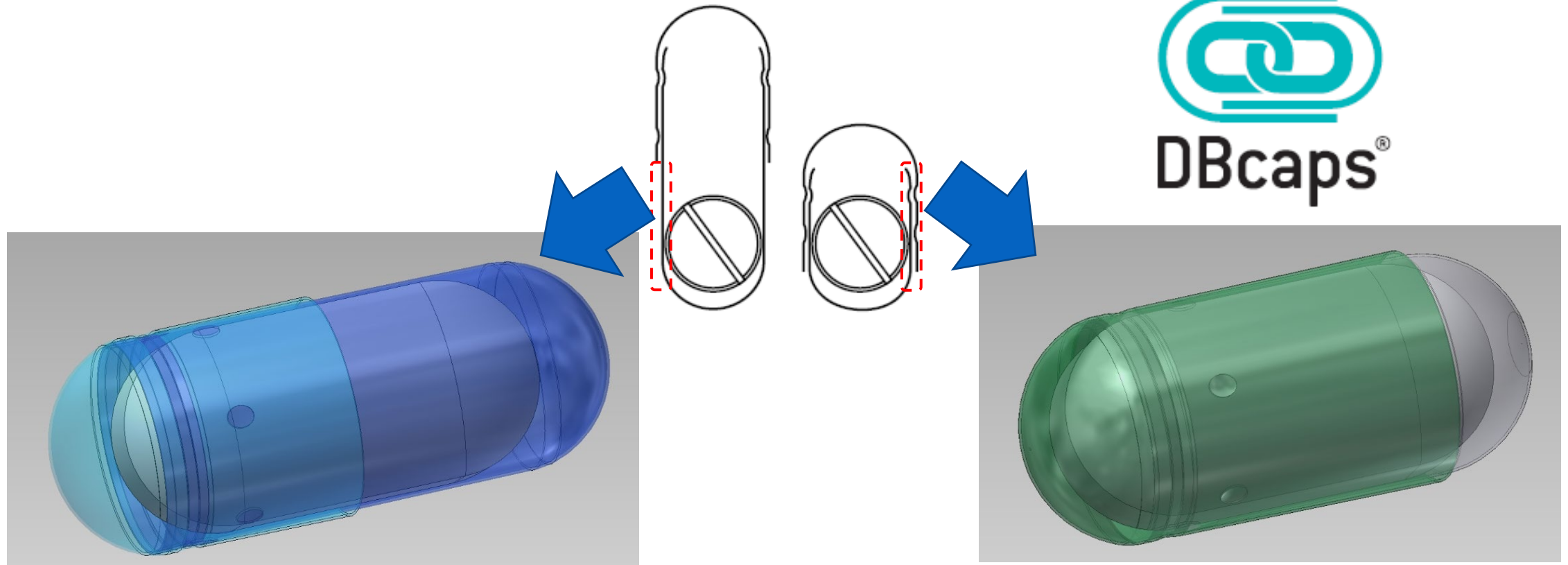
### DBcaps® capsules

- an over-encapsulation solution with a tamper evident design addressing the clinical trial challenge of testing without bias.

Features	Benefits
Wide size range available supporting over-encapsulation of 90% of marketed solid oral dosage forms	Speed to clinic, no change in dosage form properties, easy blinding process
Design with double opaque layer of cap over body	Avoid breaking the blind through visual recognition
Difficult to open for patient	Avoid breaking the blind through opening the capsule
Available in Gelatin and HPMC	Allows tuning of your study according the blinded form characteristic (hygroscopicity, prone to cross-linking).
Can be used on a wide choice of capsule filling machines – brands and outputs	Easy blinding process, speed to clinic
Compact size	Easier to swallow than standard capsule.
Limited visible body part	Original design compared to standard capsules design.

# Why use DBcaps® instead of standard capsules?

## Design is key !



Risks for **Break the Blind** linked to single layer of material on body in closed position

Unique design of cap on body in closed position assures more opacity and **reinforces the Blind**

---

# Technical insights on DBcaps® capsules



# Technical Documentation

## Dimensions and Capsule filling machine compatibility

DBCaps® capsules are available in dimensions

- Sizes AAA/AAel/AA/A/B/C/D/E in Gelatin
- Sizes AAel/AA/A in HPMC (Vcaps®Plus)

Those sizes can be filled on a large number of capsule filling equipment :

- Many brands and machine manufacturers
- Many output range :
  - from manual benchtop type
  - through semi-automated type
  - to fully automated type

**DBcaps® Capsules**  
(Capsules for  
Double-Blind clinical trials)

[illegible][illegible]



# HGC DBcaps® and HPMC DBcaps® capsules Disintegration as is

## Experimental Conditions:

- Test Items:
  - 6 Size A Gelatin DBcaps® capsules filled with 50% Lactose/50% Microcrystalline Cellulose
  - 6 Size A HPMC DBcaps® capsules filled with 50% Lactose/50% Microcrystalline Cellulose
- Disintegration testing conducted per EP and USP specifications on Sotax DT2, by visual observation
- Media : USP purified water maintained at 37±1°C
- The rupture time reported is the time at which the first of the six capsules ruptured and the complete disintegration time is the time at which all the fill material has been released from all six capsules and only fragments of shell material remain on the wire mesh of the disintegration baskets.

## Result and outcome

Capsule	First Rupture (Min:sec)	Complete Disintegration (Min:Sec)
Gelatin DBcaps®	1:35	4:58
HPMC DBcaps®	1:36	4:43

- **Both capsule types exhibit conform and similar disintegration behaviors.**

# HGC DBcaps® and HPMC DBcaps® capsules

## Disintegration - Application test with Capsule and Backfill

### Experimental Conditions:



- Test Items:
  - 6 Size 3 gelatin Colorista® capsules filled with 99.9% Lactose/0.1% FD&C Blue 2 Dye and encapsulated in size A Gelatin DBcaps® Capsules filled with 50% Lactose/50% Microcrystalline Cellulose
  - 6 Size 3 gelatin Colorista® capsules filled with 99.9% Lactose/0.1% FD&C Blue 2 Dye and encapsulated in size A HPMC DBcaps® Capsules filled with 50% Lactose/50% Microcrystalline Cellulose
- Disintegration testing conducted per EP and USP specifications on Sotax DT2, by visual observation
- Media : USP purified water maintained at 37±1°C
- The rupture time reported is the time at which the first of the six capsules ruptured and the complete disintegration time is the time at which all the fill material has been released from all six capsules and only fragments of shell material remain on the wire mesh of the disintegration baskets.

### Result and outcome

Capsule	First Rupture (Min:sec)	Complete Disintegration (Min:Sec)
Capsule placed inside Gelatin DBcaps®	Outer Capsule: 1:30 Inner Capsule: 3:36	5:45
Capsule placed inside a HPMC DBcaps®	Outer Capsule: 1:56 Inner Capsule: 3:51	5:57

- Both capsule types also exhibit conform and similar disintegration behaviors when used in an application based hypothesis

# HGC DBcaps® and HPMC DBcaps® capsules

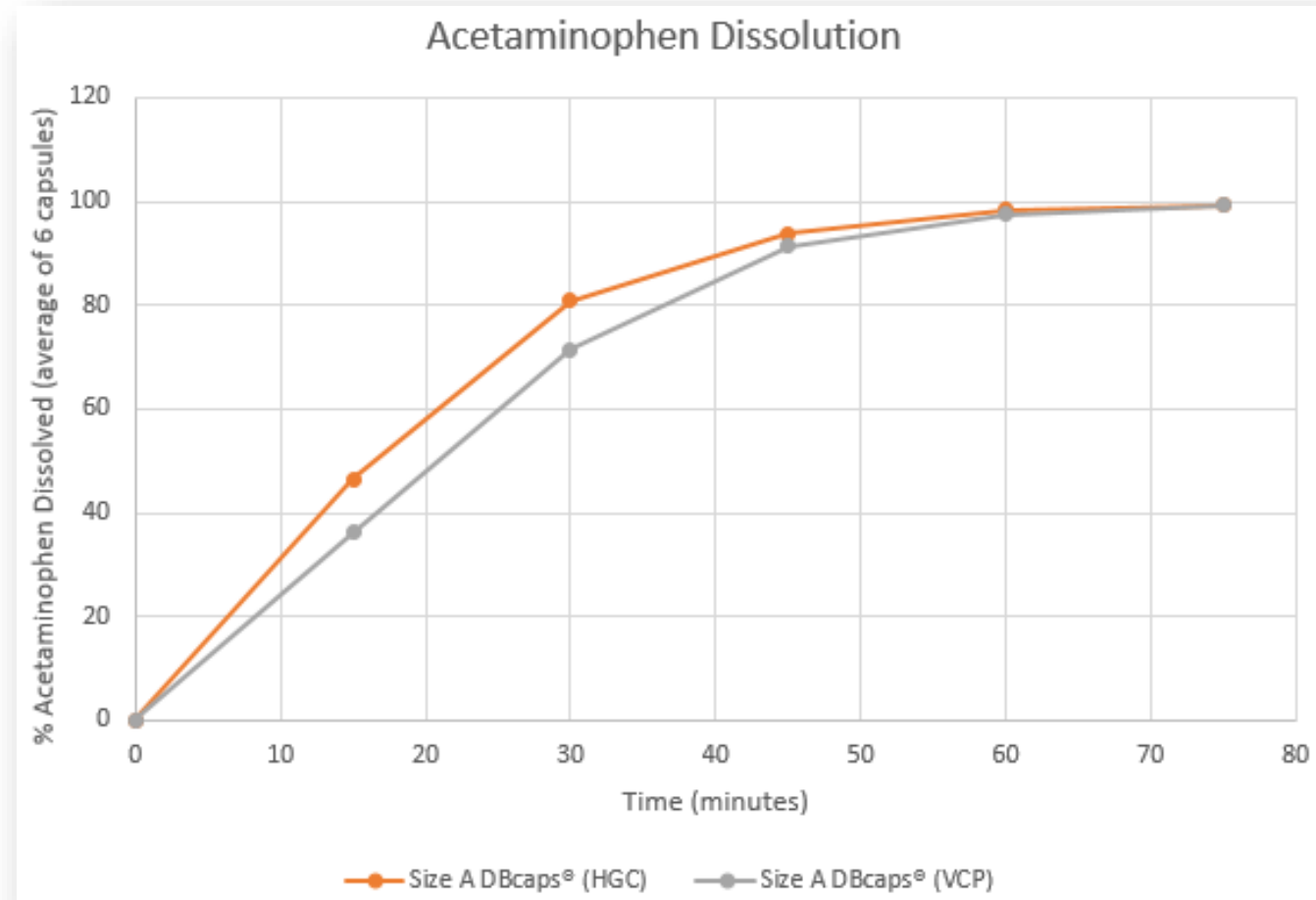
## Dissolution as is – Acetaminophen fill

### Condition of test :

- Water, 37°C
- Capsules filled with acetaminophen
- Specification for Q : 75%

### Results :

- Both polymers exhibit conform dissolution curves
- Small lag time is observed for HPMC version, related to known Vcaps Plus phenomena
- Study needs to be completed with a realistic application-oriented test.



Study conducted by Lonza

# HGC DBcaps® and HPMC DBcaps® capsules

## Dissolution - Application test with Capsule and Backfill

### Condition of test :

- Water, 37°C
- Size 3 HGC Colorista capsules filled with acetaminophen, placed in Size A DBcaps®, with Celulose/Lactose backfill material
- Specification for Q : 75%

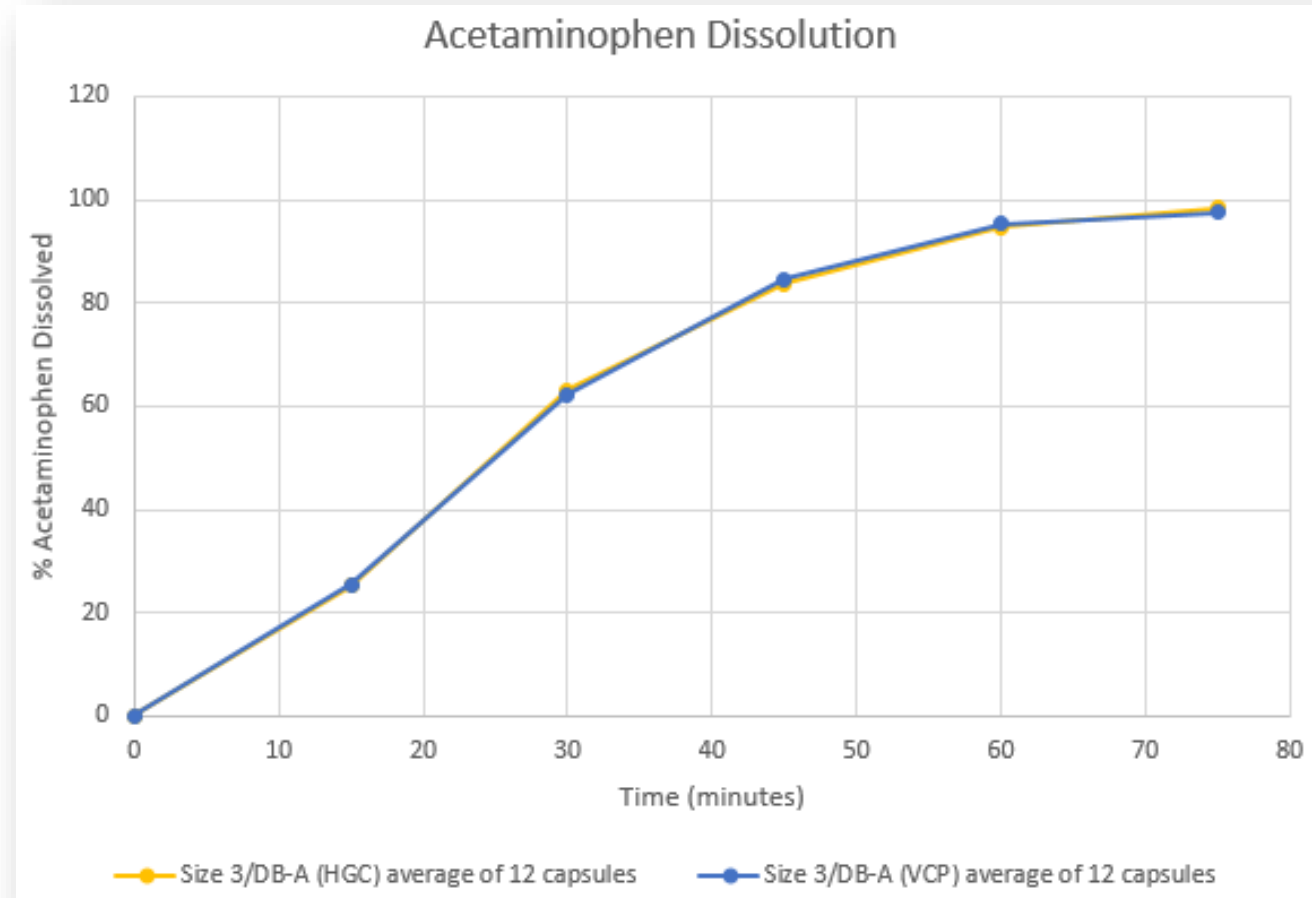


### Results :

- Both polymers exhibit conform & identical dissolution curves : the polymer nature does not affect the dissolution properties of the blinded form that has been placed inside.

**Outcome** : polymer choice for a double blind study is then linked to possible interactions :

- Water sensitive formulation
- Formulation that is prone for cross-linking phenomena
- In-vitro dissolution curves versus comparator



Study conducted by Lonza

# Decision tree

## Gelatin DBcaps® or HPMC DBcaps® ? Sizes AA/AAel/A

Properties and profile of  
Solid Oral Dosage Form to be blinded

Hygroscopic or  
sensitive to moisture ?



HPMC  
DBcaps®



Gelatin  
DBcaps®

Prone to promote  
cross-linking issues ?



HPMC  
DBcaps®



Gelatin  
DBcaps®

Global reach for the  
Double Blind Clinical Trial  
(cultural/diet/religious) ?



HPMC  
DBcaps®



Gelatin  
DBcaps®

---

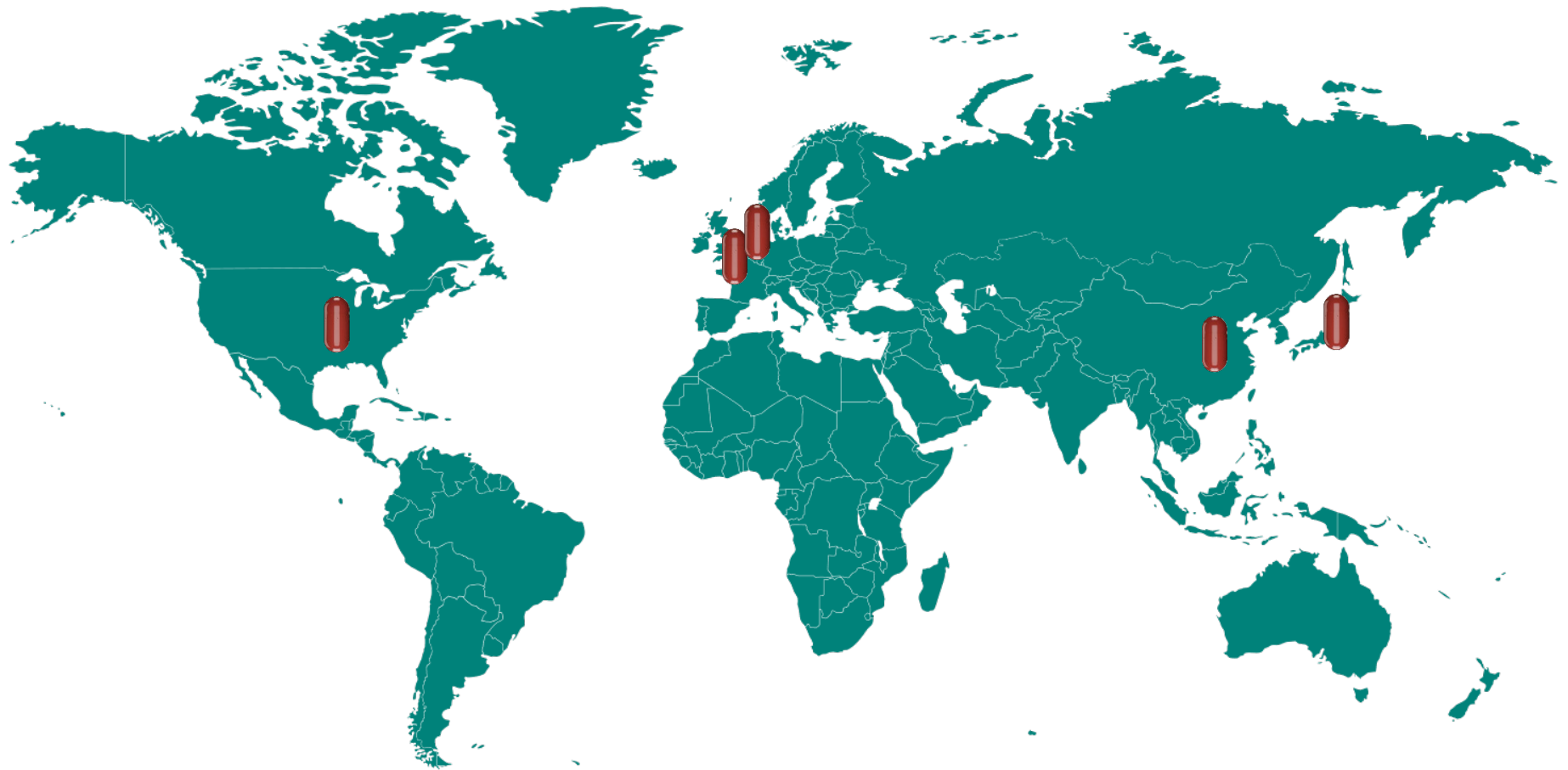
How can we support your  
upcoming clinical trials  
and developments ?





# DBcaps<sup>®</sup> source and distribution

DBcaps<sup>®</sup> capsules are produced in **USA, Belgium, France, China and Japan** and can be delivered **worldwide** thanks to our supply chain network.



# Available for your next Clinical Trial



## Size kit

- Box with multiple sizes of capsules
- Allow choosing the right capsule size for your next clinical trial
- Not intended for clinical trials



## CapsuleCaddy™

- CoA included
- 2 500 to 33 000 capsules per caddy
- Polypropylene container. Inner bag protects capsules from contamination
- Suitable for clinical trials



## Full Box

- CoA included
- 50 000 to 250 000 capsules per box
- Fiber Free box. Inner bag protects capsules from contamination
- Suitable for clinical trials

# Want to know more?

Order your complimentary DBcaps® Size kit.



Visit our website to learn more about the Capsugel® pre-clinical and clinical product lines and the solutions they offer to each stage of the development process.

Contact us to be put in touch with a regional representative to discuss which clinical solution is right for your product.

**[www.capsugel.com](http://www.capsugel.com)**  
**Made better. By science.™**

# Legal Disclaimers

**Review and follow all product safety instructions.** The statements made in these materials have not been evaluated by the U.S. Food and Drug Administration or any other regulatory authority. Lonza's products are not intended for use to diagnose, treat, cure or prevent any disease. All information in this presentation corresponds to Lonza's knowledge on the subject at the date of publication, but Lonza makes no warranty as to its accuracy or completeness and Lonza assumes no obligation to update it. All information in this presentation is intended for use by recipients experienced and knowledgeable in the field, who are capable of and responsible for independently determining the suitability and to ensure their compliance with applicable law. Proper use of this information is the sole responsibility of the recipient. Republication of this information or related statements is prohibited. Information provided in this presentation by Lonza is not intended and should not be construed as a license to operate under or a recommendation to infringe any patent or other intellectual property right. All trademarks belong to Lonza or its affiliates or to their respective third parties and are used here only for informational purposes. Copyrighted material has been produced with permissions or under license, all other materials © 2020 Lonza.



# — Questions —



———— **Thank You** ————