

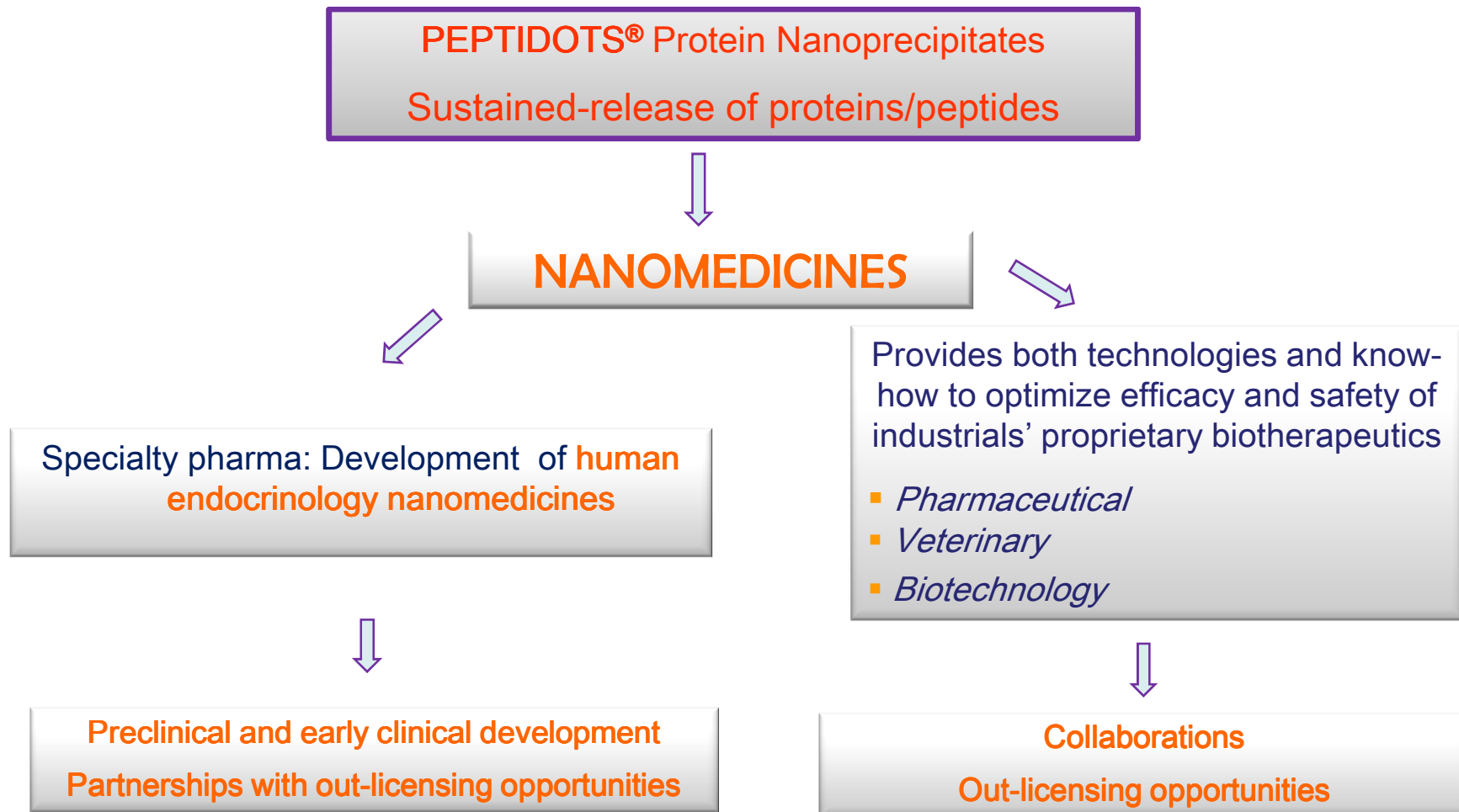


CarlinaTechnologies
Micro & nano encapsulation platforms

Innovation in the controlled delivery of therapeutic proteins

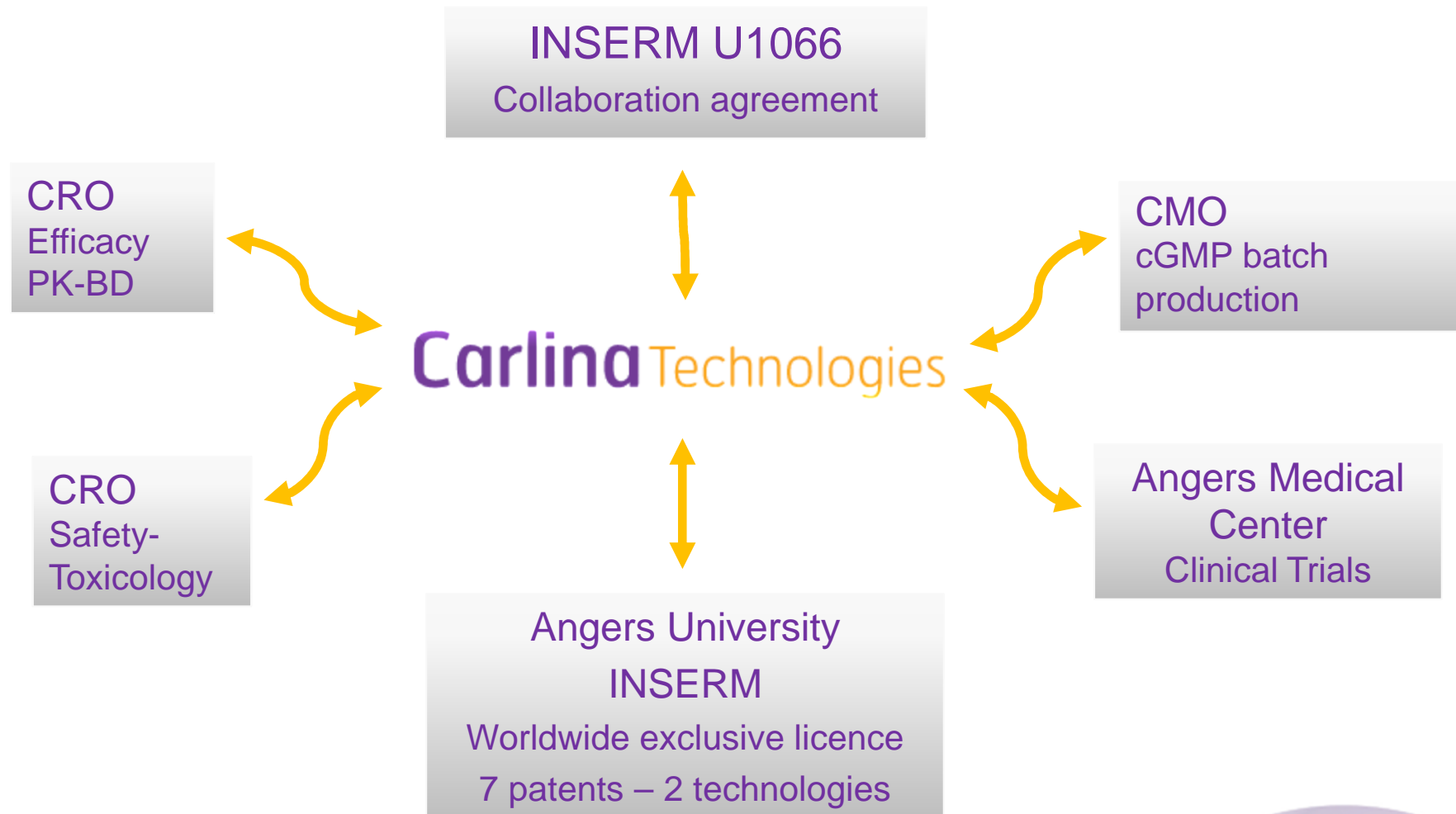
Activities and Business Model

Proprietary drug delivery platforms initially developed at University of Angers and INSERM





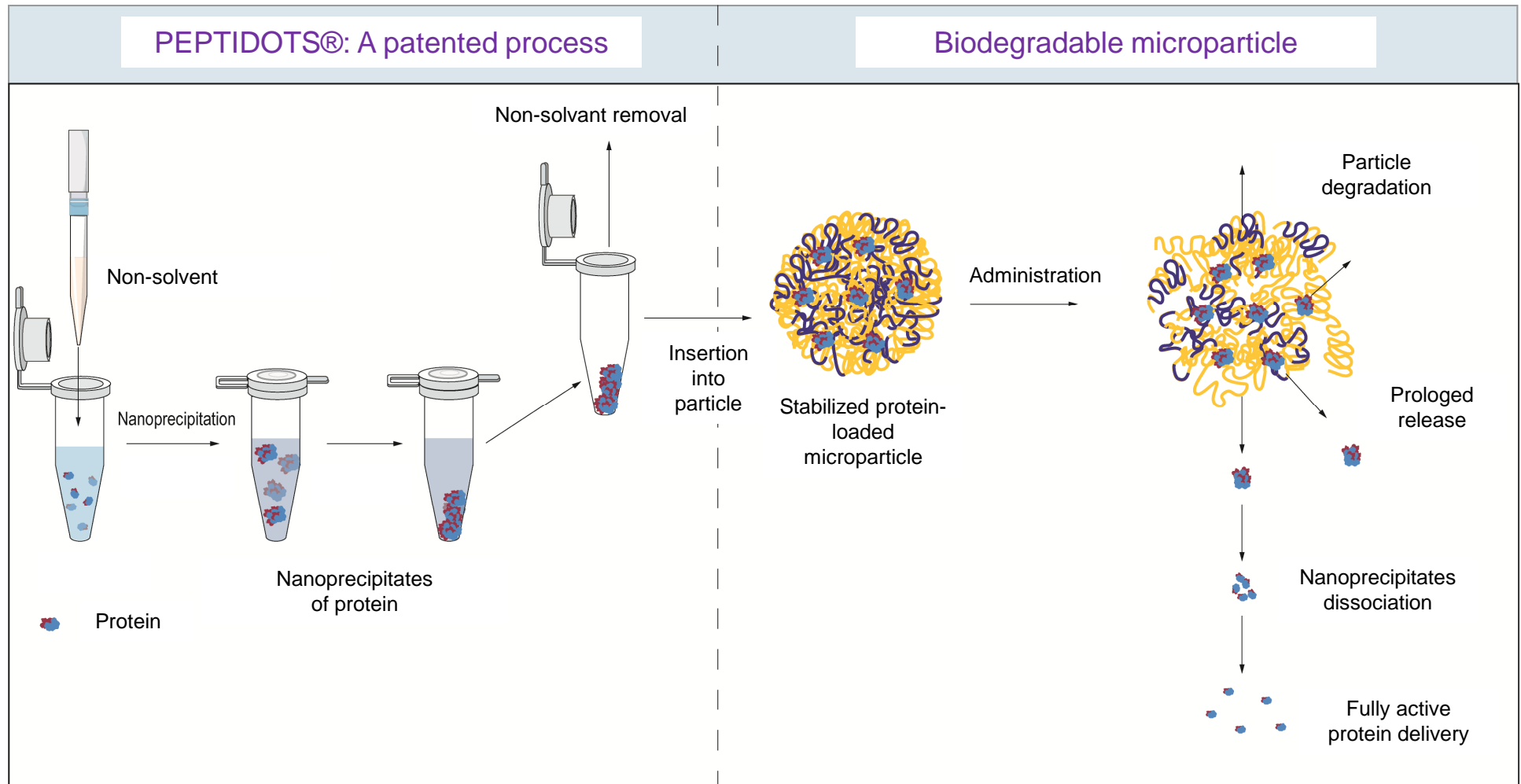
Partners



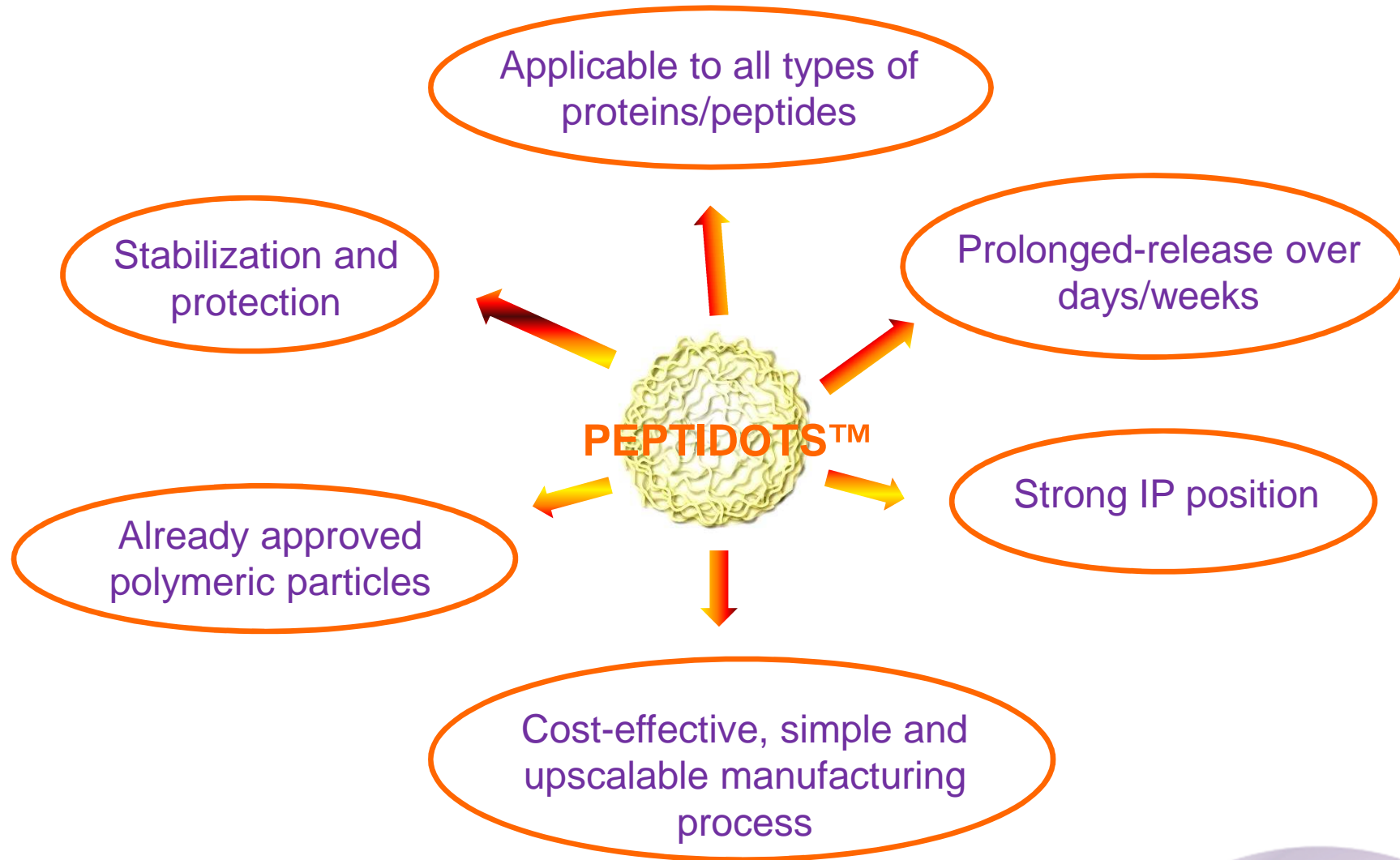
PEPTIDOTS: A unique technology platform

STABILIZATION OF PROTEINS BY NANOPRECIPITATION

NON-DENATURING ENCAPSULATION AND PROLONGED-RELEASE

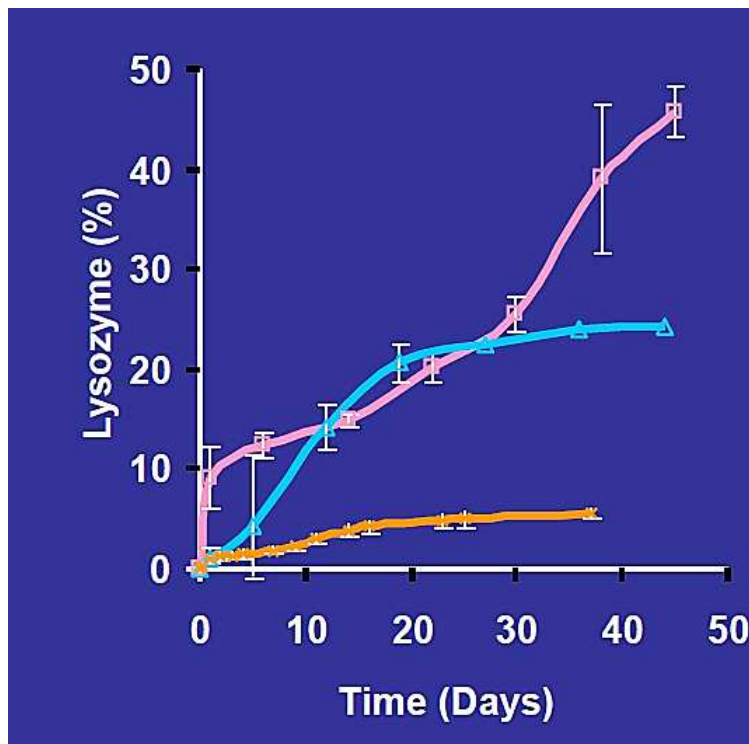


PEPTIDOTS: Fills the gap for lack of non-denaturing protein encapsulation methods

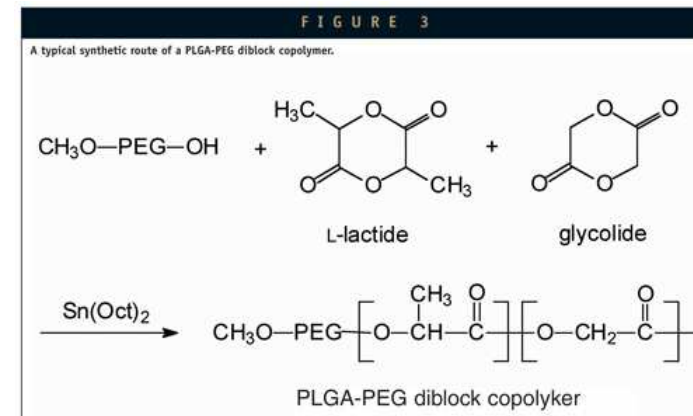


Sustained release of proteins & peptides

	β -galactosidase	Peroxydase	α -chymotrypsine	Lysozyme
Total	84 \pm 6%	89 \pm 7%	94 \pm 3%	72 \pm 5%
Actif	78 \pm 1%	82 \pm 5%	Interférences	71 \pm 4%
Actif / total	93%	92%	-	99%



- Lysozyme-ploxamer 188 in PLGA-PEG-PLGA
- Lysozyme-ploxamer 188 in PLGA
- Lysozyme in PLGA



Sustained release of proteins & peptides

Model proteins:

Lysozyme

α -chymotrypsin

Peroxidase

β -galactosidase

Therapeutic proteins:

VEGF

Hepatocyte growth factor

Insulin-like growth factor

Erythropoietin

IL-2

Insulin

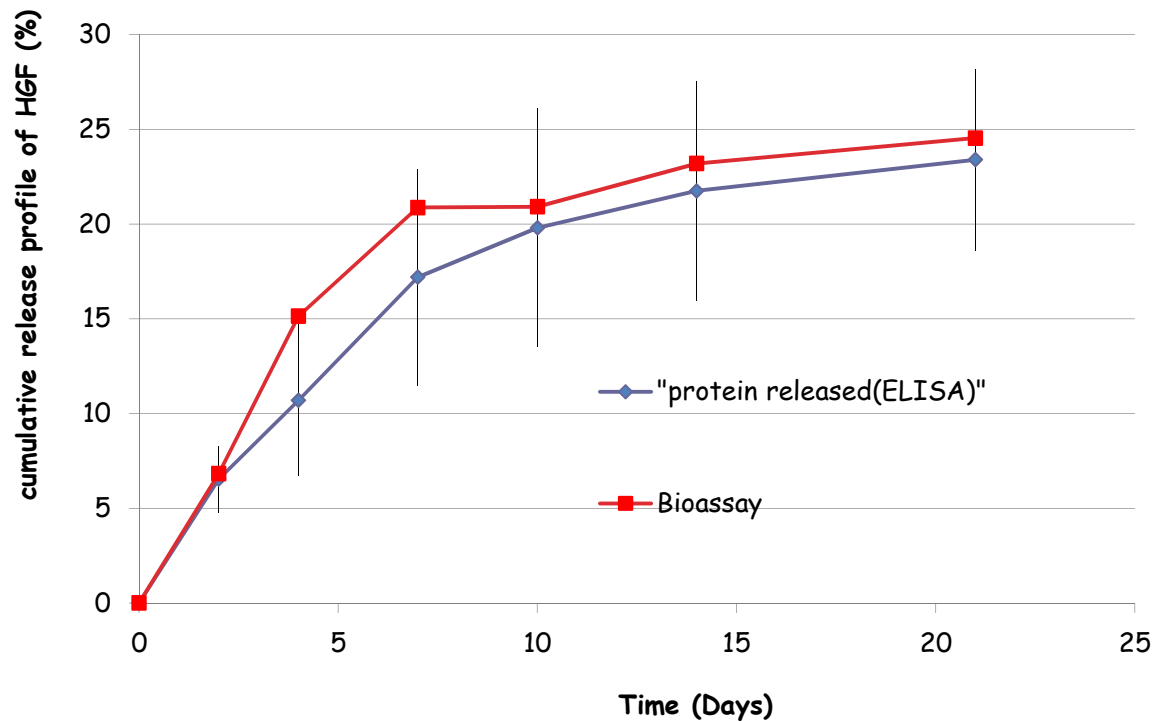
Antibodies

Growth hormone

PEPTIDOTS - Hepatocyte Growth Factor

Encapsulation efficiency: 83.5% (NanoOrange test)
82% (ELISA test)

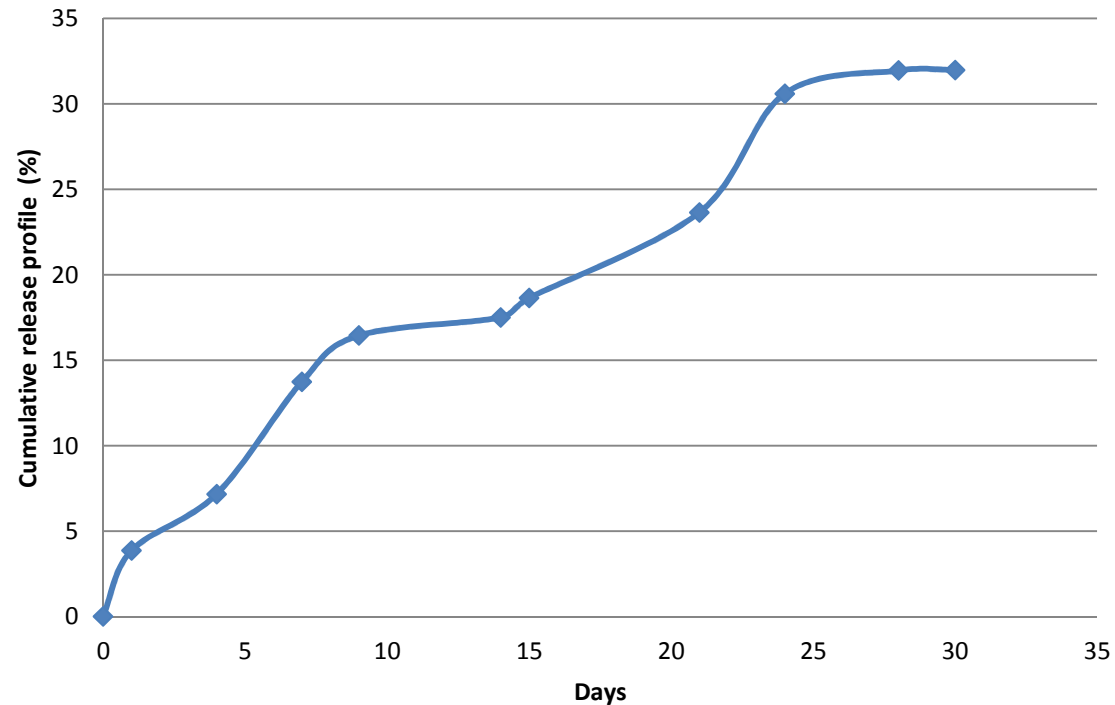
In vitro release of nanoprecipitates of hepatocyte growth factor



PEPTIDOTS-Insulin-like Growth Factor 1*

Encapsulation efficiency: 69% (ELISA test)

In vitro release of nanoprecipitates of IGF1

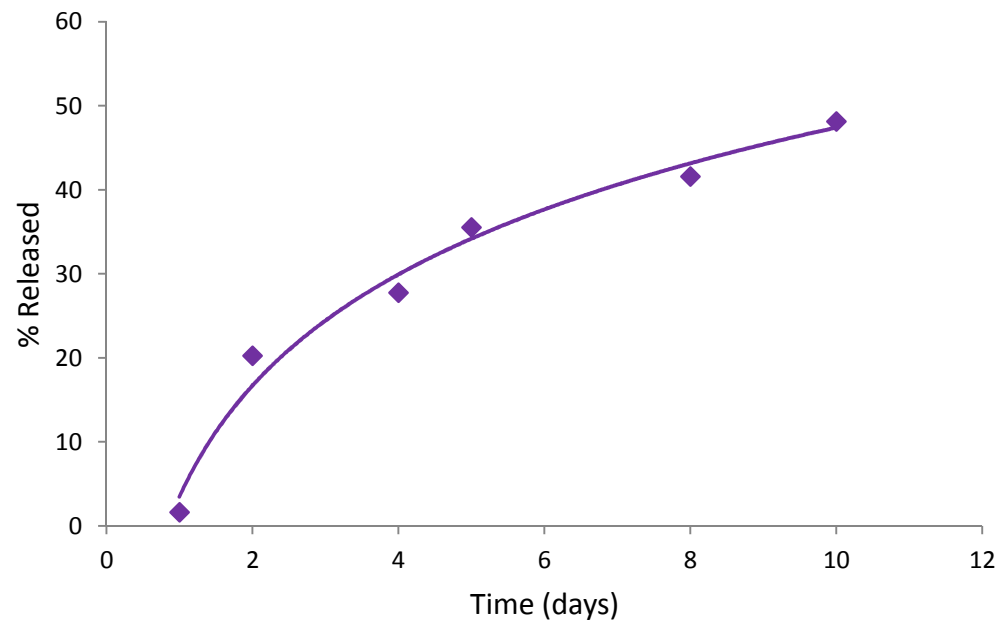


* Non optimized formulation

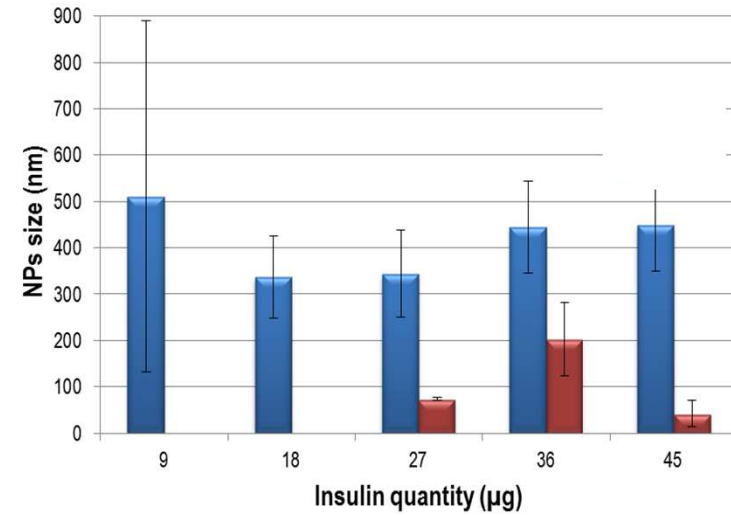
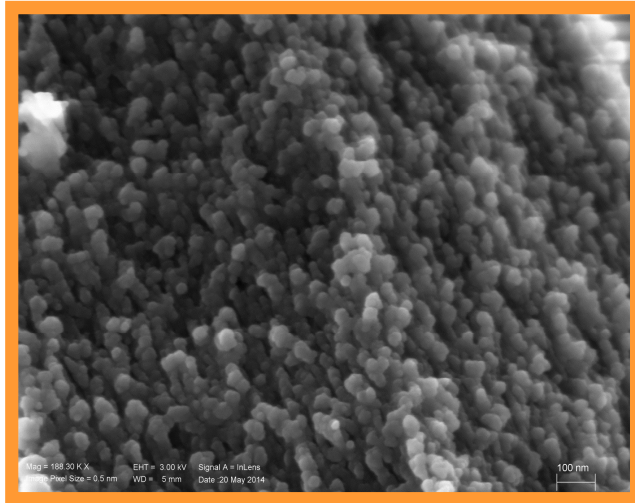
PEPTIDOTS-interleukin2

In vitro release of nanoprecipitates of IL-2

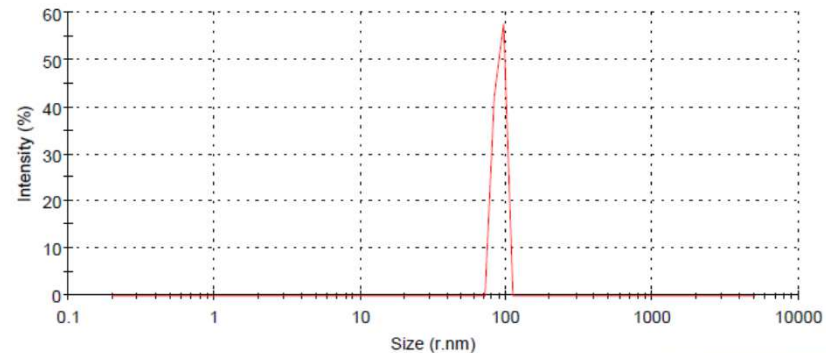
Polymeric gel
up to 100% entrapment efficiency



PEPTIDOTS-insulin: Nanoprecipitation of insulin



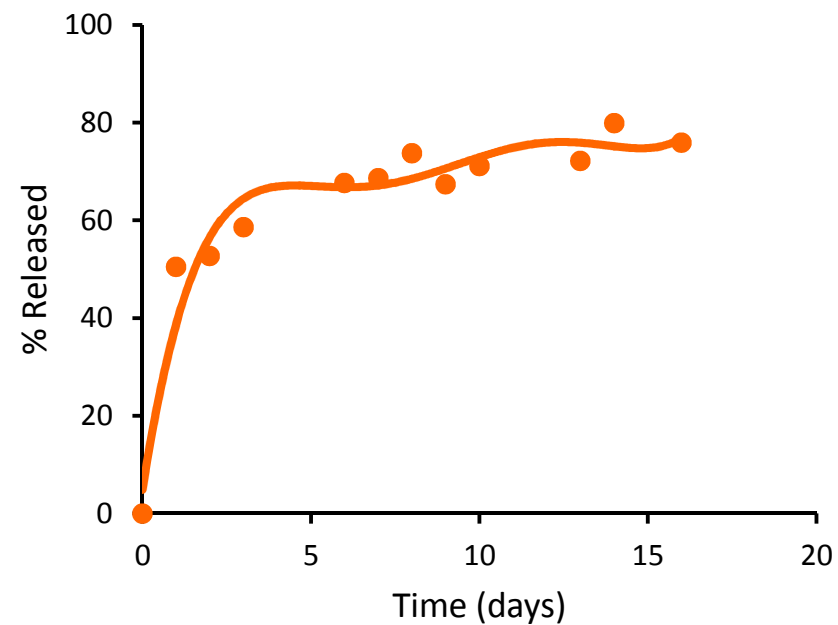
*Nanoprecipitates
up to 100% yield
 $\varnothing \leq 100 \text{ nm}$*



PEPTIDOTS-insulin

In vitro release of nanoprecipitates of insulin

Polymeric gel
up to 100% entrapment efficiency



Animal model used for *in vivo* PoC

Handling Procedure

The handling of our VAH access system is easy. The catheter is connected to a chamber contained in a silicone harness, which is worn in the interscapular region by the animal. The septum of the harness should be cleaned before and after each sampling or injection session.

One person should gently restrain the animal, while another works with the catheter.



Animal handling



Overview of the chamber



Removing of the cap

1/ The cap is removed and the septum is cleaned with an aseptic solution (chlorhexidine).



Sampling

2/ The lock solution is removed by gently withdrawing with a sterile 1-mL syringe (1). When withdrawing, the lock solution is immediately mixed with blood.

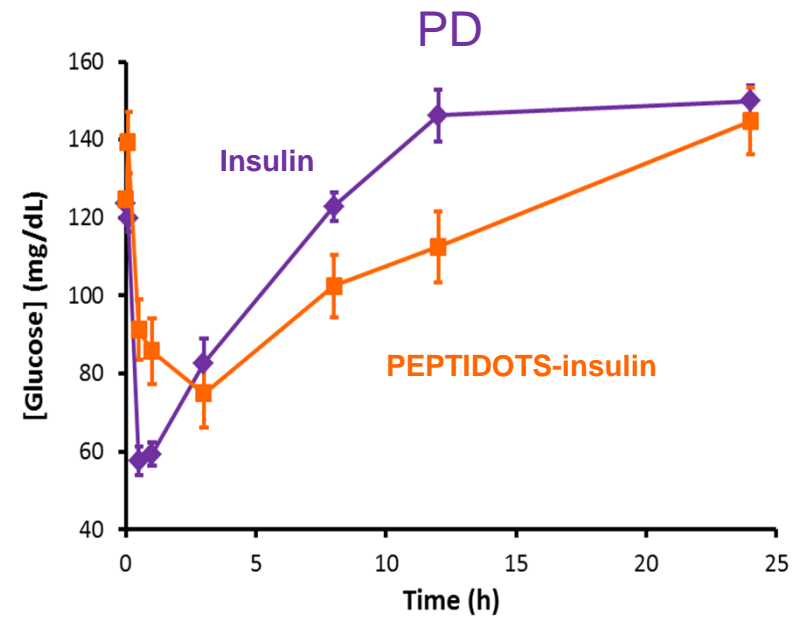
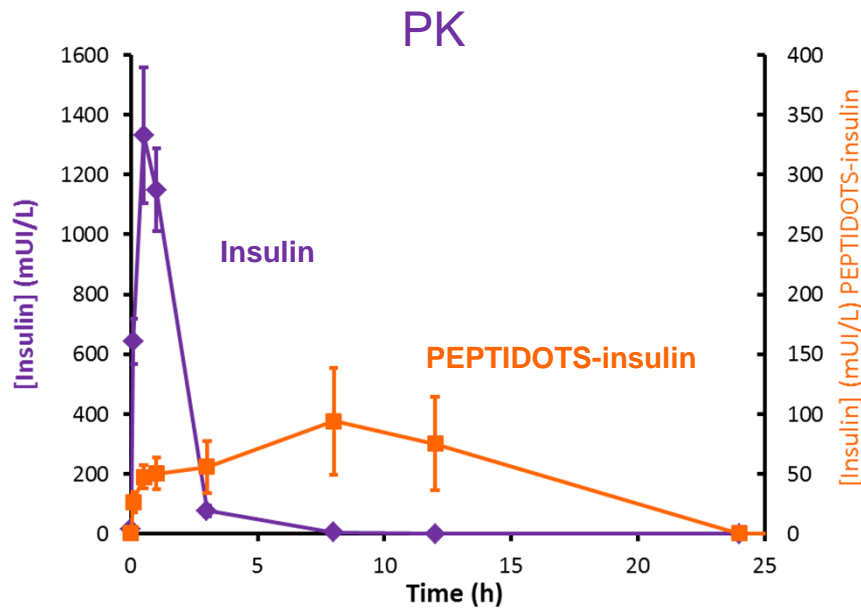
If the first attempt fails:

- The position of the catheter should be changed in the subcutaneous pouch by massaging the scapular region or changing the position of the forelimbs of the animal, and then the procedure can be tried again.
- A small amount of sterile saline (0.1 mL) is injected to clear the catheter, and then the operation can be repeated.

3/ The syringe (4 or 5) is connected (with a blunted needle) for sampling or injection.

PEPTIDOTS-insulin: *in vivo* Proof-of-concept

Insulin nanoprecipitates in polymeric matrix vs. non-formulated insulin



	Starting	Duration	C min	Onset
insulin	30 min.	8 h	58 mg/dL	30 min.
PEPTIDOTS	30 min.	24 h	75 mg/dL	3 h

- PEPTIDOTS-insulin shows a 3-fold increased PK and duration of action over non-formulated insulin in rats following s.c. administration

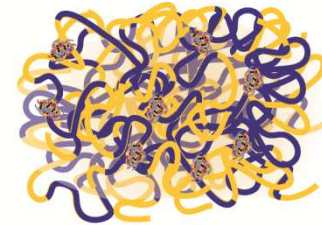
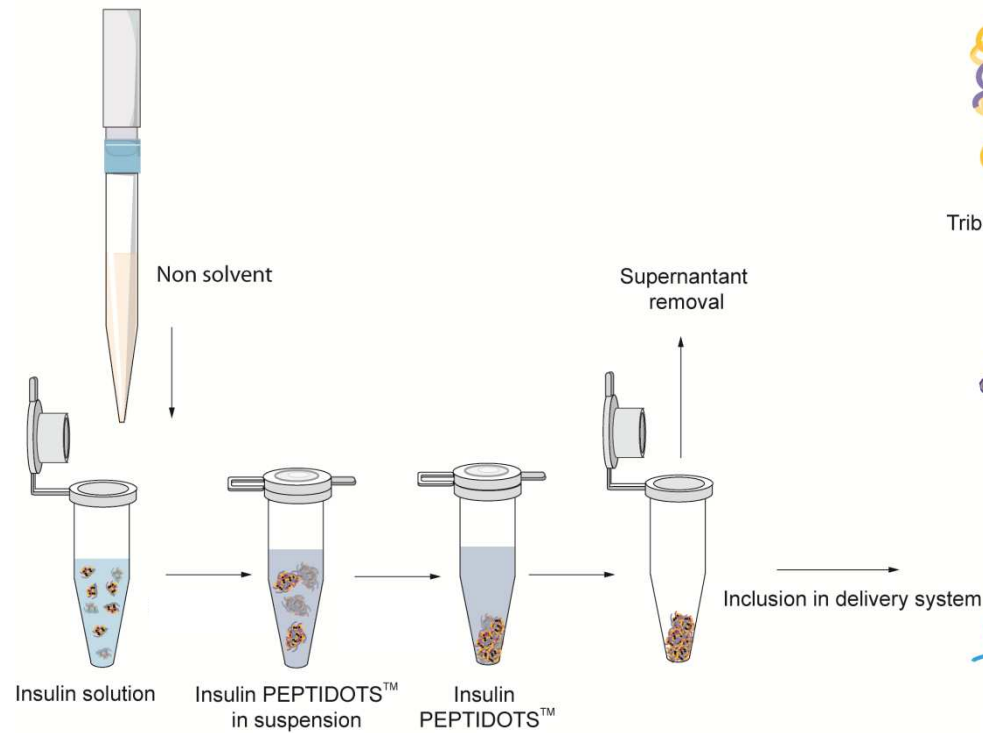


PEPTIDOTS-insulin: *in vivo* Proof-of-concept

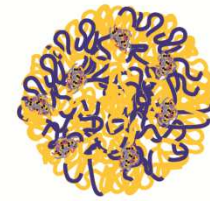
- ✓ Formulated nanoprecipitated insulin (Humulin R) is active
- ✓ Show a drastic change in PK profile over non-formulated insulin
- ✓ No modification of starting time of action post-administration (30 min.)
- ✓ Show a 3-fold increase in duration of action (effect on glycemia)
- ✓ Expected reduced risk of hypoglycemia upon s.c. injection – no burst effect
- ✓ No signs of general toxic side effects observed, including at injection site

- ❑ Room for improvement to achieve further increased duration of action through formulation optimization, i.e. polymeric matrix and delivery system used

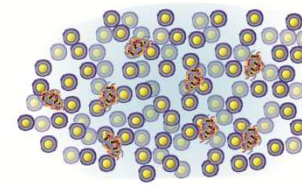
PEPTIDOTS-Insulin: new formulations for insulins and their derivatives



Triblock copolymer organogel



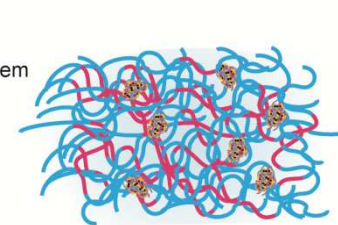
Triblock copolymer microparticle



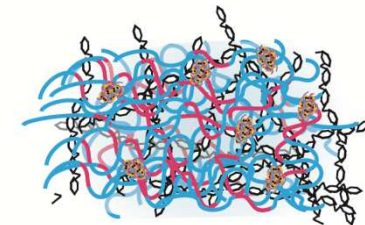
SOLUDOTS™ based gel



Triblock copolymer nanoparticle



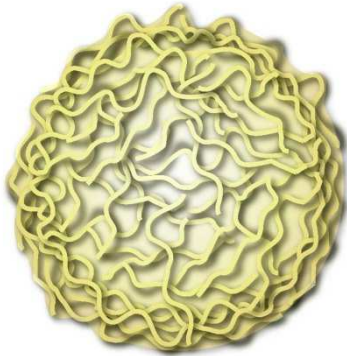
Polymeric gel



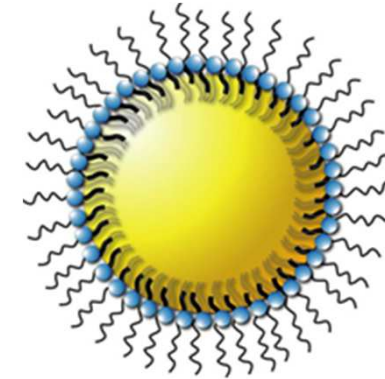
Mixed polymeric gel

PEPTIDOTS

Applicability of our PEPTIDOTS
technology to your proprietary
therapeutic proteins/peptides



Thank you !



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Un réseau. Un esprit

