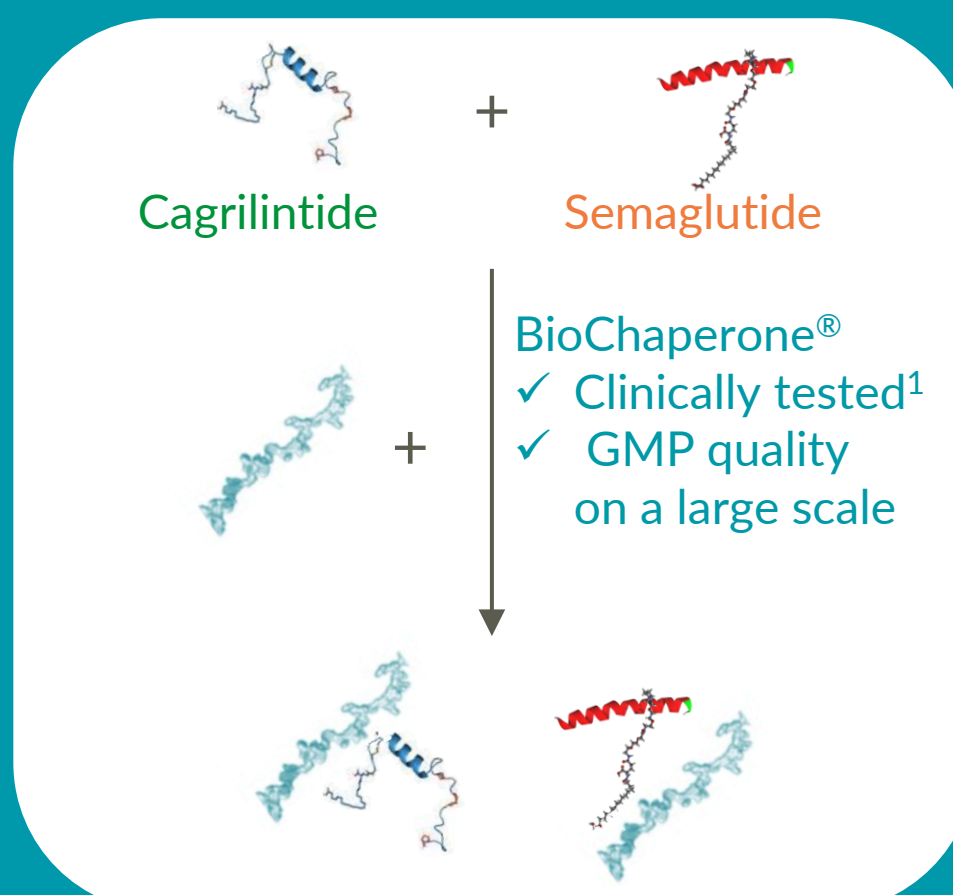




- BioChaperone® is designed to solve formulation stability and performances issues.
- Co-formulation of Cagrilintide and Semaglutide is hindered by limited compatibility in solution.
- BC forms reversible molecular complexes with both API via non-covalent interactions.
- Formulation manufacturing is a standard liquid process with fill & finish into cartridges.

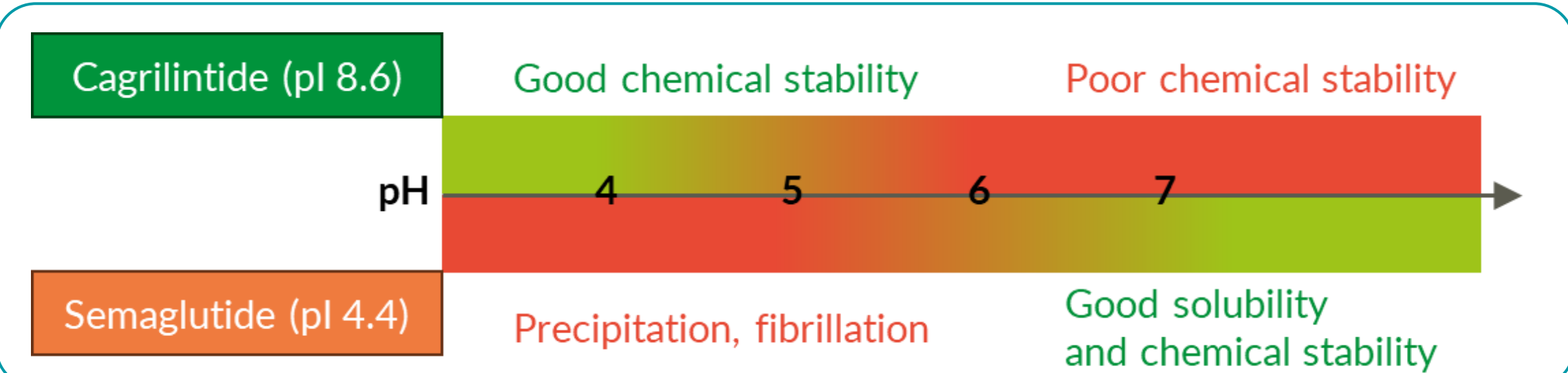


- BC CagriSema demonstrated good chemical and physical stability suitable for commercial use.
- Antimicrobial efficacy testing demonstrated suitability for use in multiple-use flexible dose pen injector.
- PK study in minipig showed similar exposure for both peptides compared to separate injections.
- BioChaperone® had good local tolerability in minipig by SC route with clinically relevant concentrations and pH.

Introduction & Background

- Key challenge with anti-obesity treatments is ensuring long-term adherence. Nearly half of patients discontinue injectable treatments within a year.
- Multi-use formulations, flexible dosing, and personalized titration strategies may enhance outcomes, reduce side effects, and increase persistence.
- Semaglutide and cagrilintide are two long-acting peptide developed by Novo Nordisk with complementary mechanisms of action. CagriSema, a combination of these peptides, is currently under phase 3 clinical evaluation³ for the treatment of diabetes and obesity using a dual-chamber device.
- There are major solubility, physical, and chemical compatibility issues that block the straightforward co-formulation of cagrilintide and semaglutide. No single pH can grant solubility, colloidal stability, resistance to amyloid fibrillation, and acceptable chemical stability see Fig. 1.

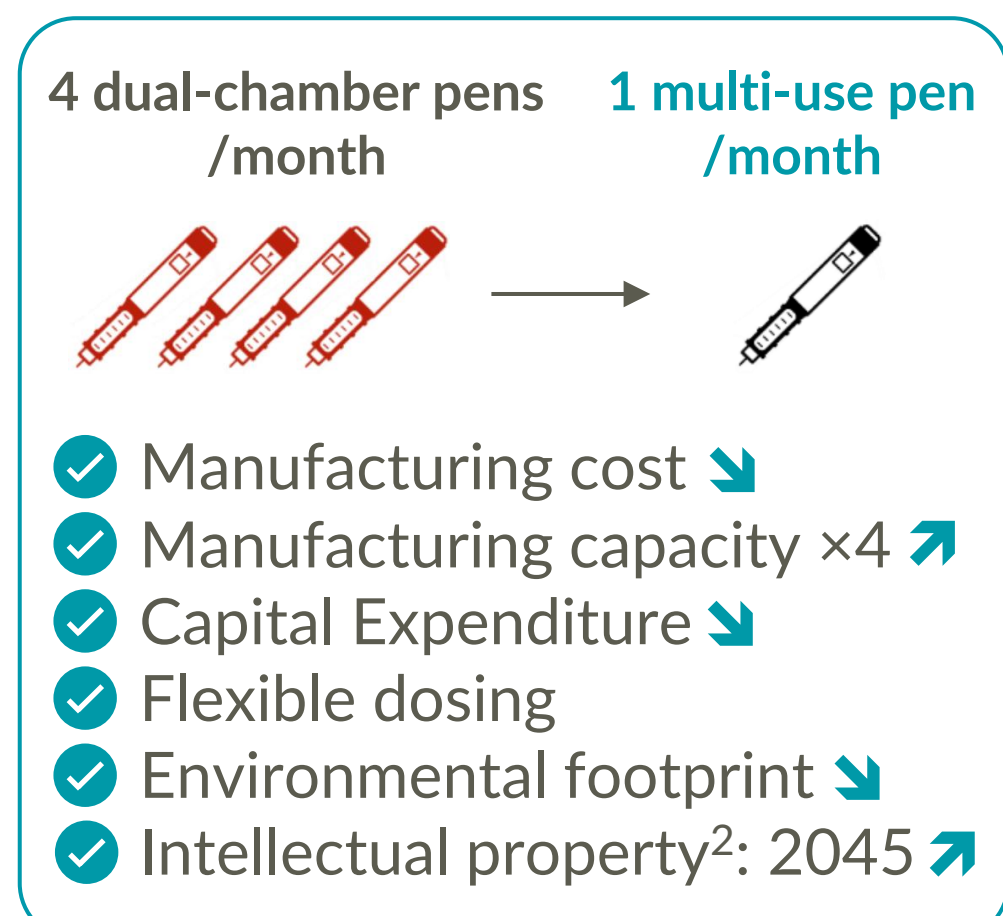
Figure 1 – Co-formulating cagrilintide and semaglutide: A Catch-22 situation



Purpose

- BC CagriSema co-formulation was developed to enable multiple-dose flexible dosing with standard pen injectors, see Figure 2.
- BioChaperone® is a proprietary pharmaceutical excipients tailored to solve formulation issues by means of aqueous non-covalent molecular complexation.
- The BioChaperone® excipient used for BC CagriSema, available in GMP-grade, is Phase-3-ready with a demonstrated CMC, ADME, toxicological and clinical history.

Figure 2 – BioChaperone® enabling power



[1] Tested on other hormonal combinations, such as NCT02514954, NCT02514850.
[2] WO2025172605 & WO2025172606. The patent term is anticipated.
[3] N Engl J Med 2025;393:635-647, N Engl J Med 2025; 393:648-659

Methods

Biophysical Characterization, Stability & AET

- Complex formation between BioChaperone® and both peptides was characterized by several orthogonal methods : BLI, DLS, CD and PAGE.
- The physical stability of the formulation was evaluated by visual inspection, ThT assay and MFI over a 28-day in-use test at 30°C.
- Chemical stability was evaluated by decrease in purity in both real time and at 37°C measured by RP-UPLC and SE-HPLC.
- Antimicrobial efficacy testing was carried out using compendial methods.

Pharmacokinetics in minipig

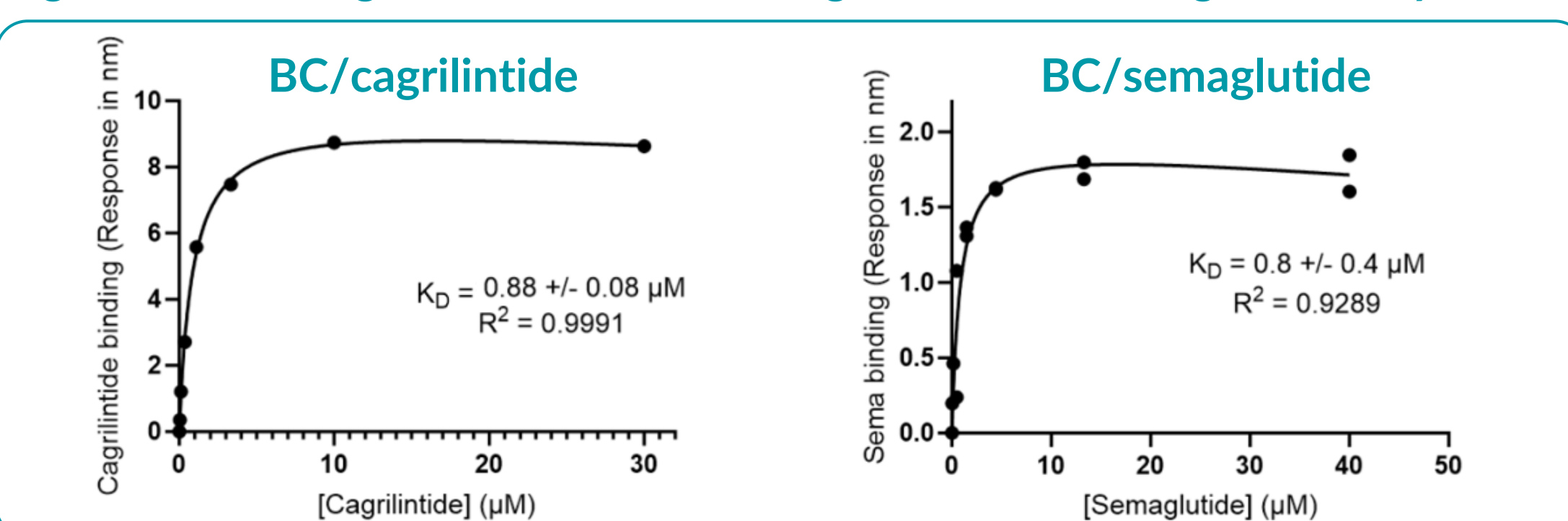
- Cagrilintide and Semaglutide PK were obtained in Göttingen naïve minipigs (N=6) following subcutaneous administration.

Results

Non-covalent interactions

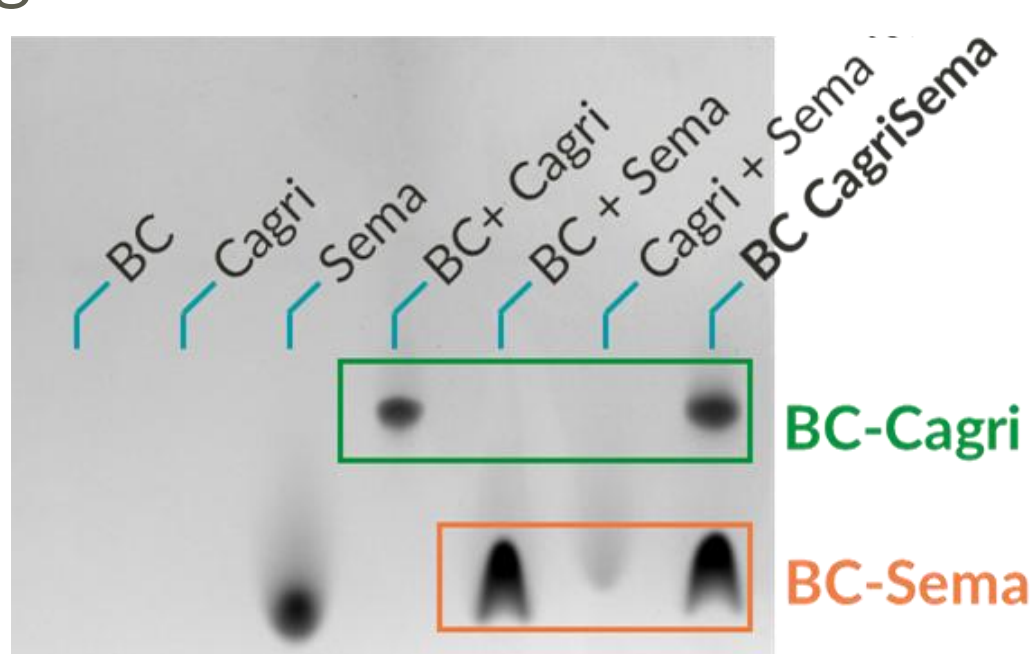
- BioChaperone® binds both peptides with sub-micromolar affinities – see Fig. 3 – that induce the formation of ≤10-nm molecular complexes loaded with more than 99% of peptides.

Figure 3 – Binding affinities of BC/semaglutide and BC/cagrilintide by BLI



- BC Cagrilintide and BC semaglutide form discrete and diffusive complexes in formulation, see Fig. 5.

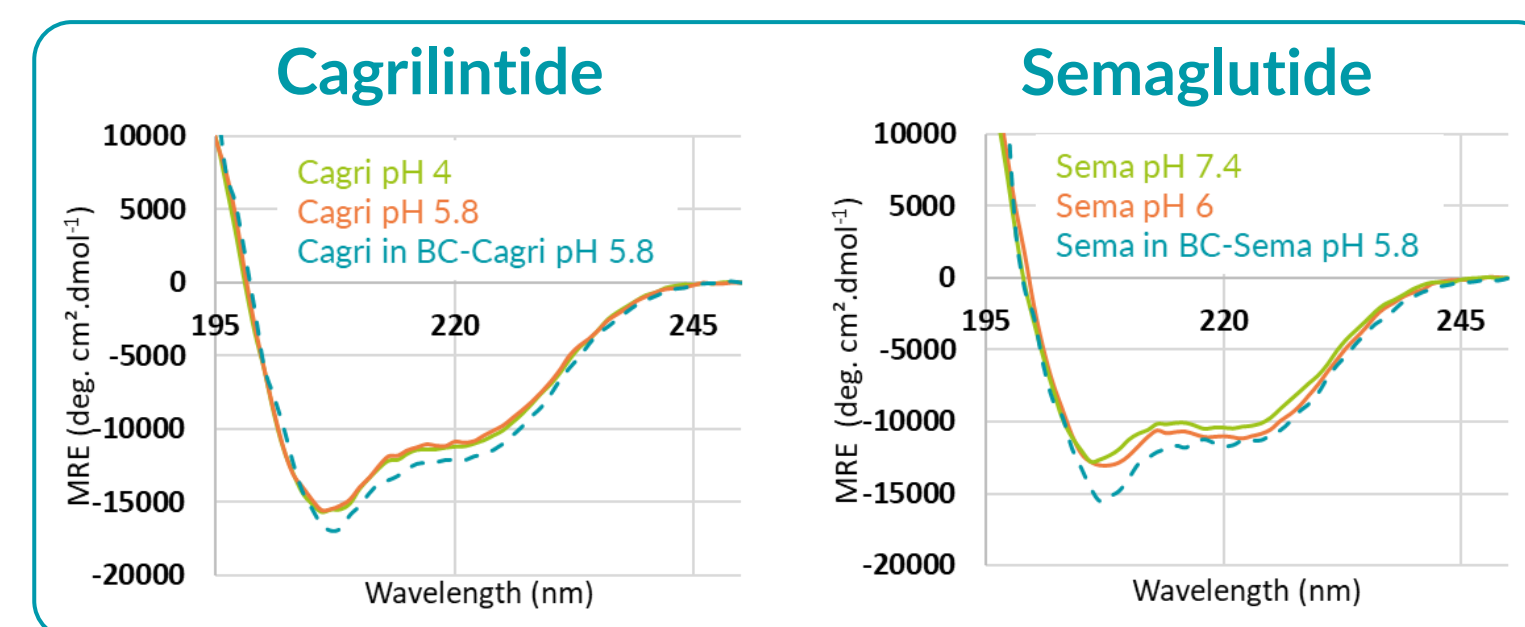
Figure 5 – PAGE illustrating how BC/cagri and BC/sema complexes are separately formed in co-formulation



Secondary structure of the peptides

- BioChaperone® maintains critical α-helix-rich structuration of both peptides (Fig. 4).

Figure 4 – Far-UV CD spectra of free and bound peptides.



BC Semaglutide stabilization

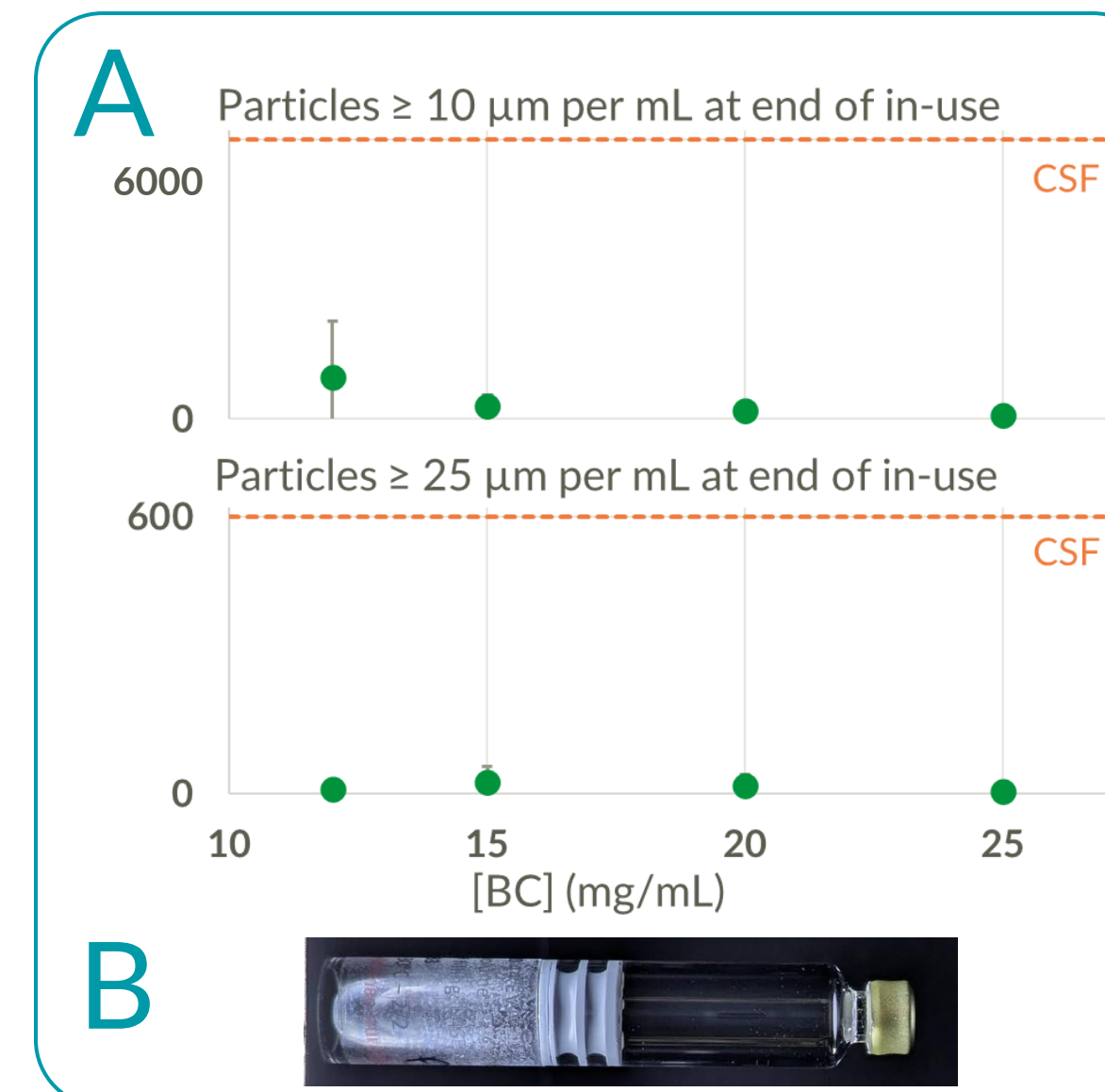
- Semaglutide quickly fibrils < pH 6.5.
- The highly charged stable BC Sema complex increases the solubility range of semaglutide, see Fig. 6.
- BioChaperone® expanded the formulation design space towards lower pH by abrogating semaglutide fibrillation below its solubility limit, see Fig. 6.

Figure 6 – Impact of pH on BC sema stabilization (ThT, 37°C)

Mean ThT lag times for BC-semaglutide solutions (h)

BC/Sema molar ratio	pH	5.6	5.8	6.0	6.2	6.4	6.6	6.8	7.0
0	Insoluble sema	1	4	7	11	19	≥99		
0.5		3	3	4	8	13	32	≥99	≥99
1		6	8	6	17	≥99	≥99	≥99	≥99
2		76	≥99	≥99	≥99	≥99	≥99	≥99	≥99

Figure 7 – A: Sub-visible particle content in cartridges after 4 weeks of simulated patient use at 30°C. B: Illustration of a cartridge of BC CagriSema



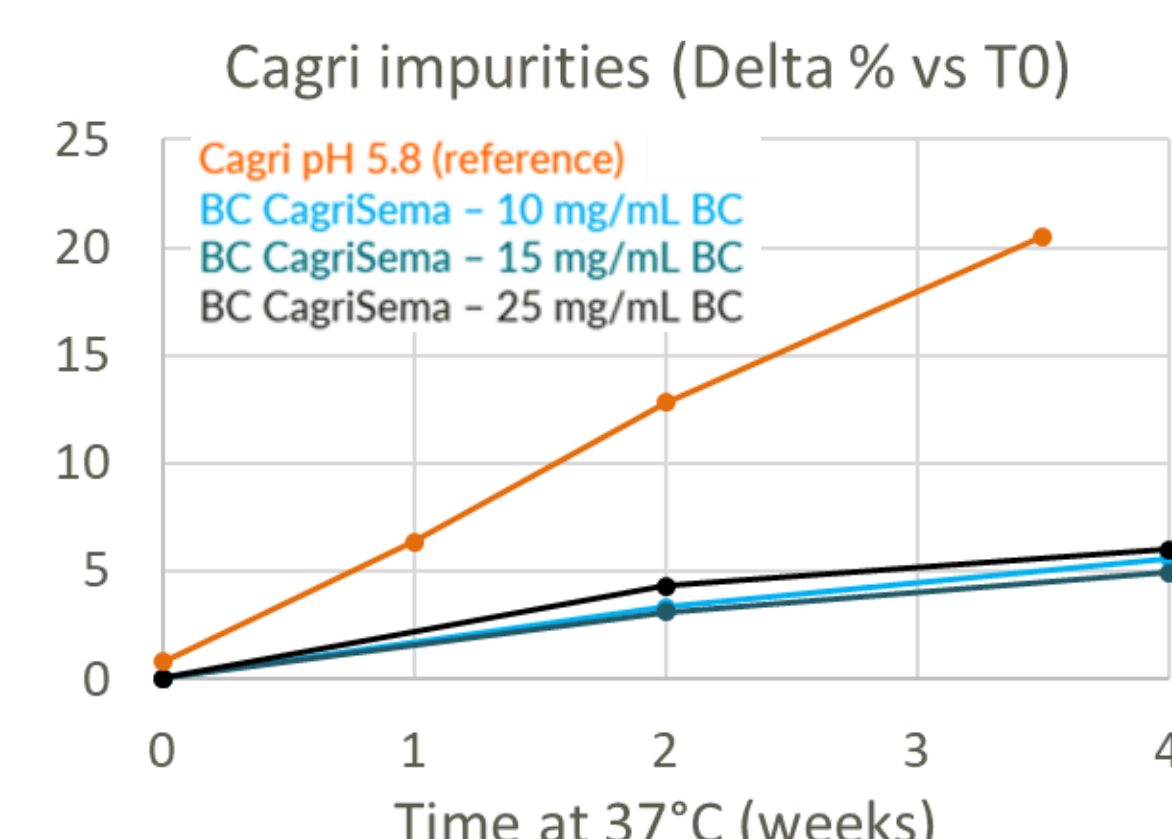
Physical stability

- BC CagriSema co-formulation composition was developed to pass physical stability stress test as assessed by ThT, visual inspection and MFI, see Fig. 7.
- Results demonstrate that semaglutide fibrillation and other physical destabilization mechanisms are robustly prevented to enable multiple injections during a month.

Chemical stability

- Chemical stability studies revealed that when enough BioChaperone® was present to grant physical stability, the recoveries and impurity profiles were solely dependent on pH, see Fig. 8.
- BioChaperone® improves cagrilintide chemical stability compared to its free form, pointing at a specific chemically stabilizing feature of this excipient.
- Real-time data at 2-8°C beyond 1 year supports recoveries >90% for both peptides after 24 months at 2-8°C of shelf life + 4 weeks at 30°C in-use.

Figure 8 – Impact of adding BC on cagrilintide chemical stability at 37°C



Preservative efficacy for multi-dose

- BioChaperone® is compatible with standard antimicrobial preservative including phenol, benzyl alcohol and *m*-cresol.
- Compendial criteria are achieved by means of BioChaperone® to enable multi-dose administration with a single cartridge in a standard pen injector (see Table 1)

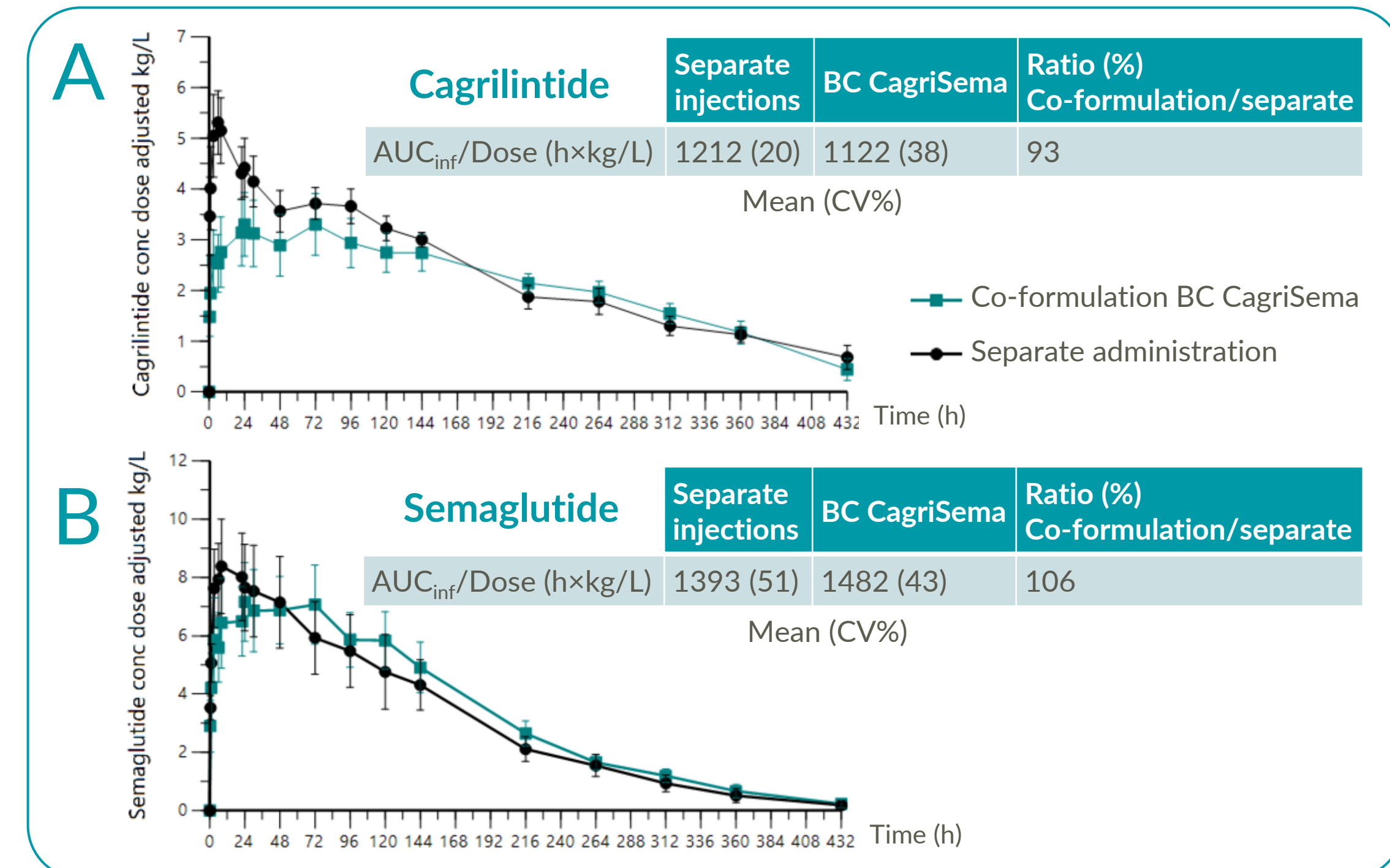
Table 1 – AET results for two co-formulations with varied BC concentration

Product strength	Preservative	Stabilizer	AET results: <i>S. aureus</i> log10 reduction					Compliance to pharmacopoeia	
APIs concentration	[<i>m</i> -cresol] (mM)	[BC] (mg/mL)	T6H	T24H	T7D	T14D	T28D	Eur.Ph.	USP
3.2 mg/mL Cagri	35	10	1.8	> 5.0	> 5.0	> 5.0	Not detected	Complies (criteria A)	Complies
3.2 mg/mL Sema		15	1.6	> 5.0	> 5.0	> 5.0	Not detected	Complies (criteria B)	Complies

Pharmacokinetics in minipigs

- BC CagriSema is easily injectable with a 30G needle. The pharmacokinetics study showed a similar exposure of each API, with a slight reduction of Cmax, see Figure 9.
- The non-covalent reversible BC/API complex unbinding mechanism is triggered both by competition with albumin and by dilution, ensuring a good release of APIs after administration.
- Safety data obtained indicated good tolerance at injection site.

Figure 9 – Mean (± SE) pharmacokinetic profiles of cagrilintide (A) and semaglutide (B) after a single SC injection of BC CagriSema, or separate injections of free cagrilintide and free semaglutide in minipigs (N=6)



Conclusions

- The physical and chemical stability success criteria achieved demonstrate how the BioChaperone® technology enables the co-formulation of cagrilintide and of semaglutide for administration in multiple-use and flexible dose pen injectors.
- The BioChaperone® technology has a demonstrated track record for preserved acylated peptides and other difficult-to-formulate peptides.