PharmaShell® –

The high drug load delivery system enabling the next generation long-acting injectables through atomic layer precision

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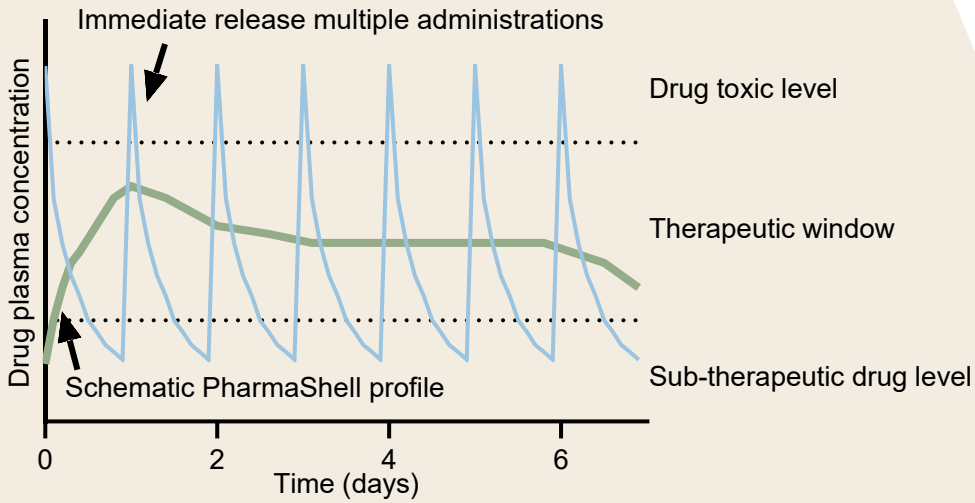
About Nanexa

- **Nanexa** is a fully integrated drug development company specializing in Long Acting Injectables (LAIs) based on the proprietary PharmaShell® drug delivery system
- **Positive Proof of Concept** with Phase 1 data on NEX-22, a long-acting formulation of liraglutide for the treatment of type 2 diabetes
- **Patent portfolio** that encompasses key enablers of producing LAIs using the technology
- **Attractive partner** for development of long-acting injectables able to supply partner with CTM
- **Management team** with long experience in pharma

PharmaShell® LAI enables smarter care



Drugs with short half-life are transformed into long-acting injectables with improved properties

Drug concentrations are maintained within the therapeutic window for optimal benefit

PATIENTS

- Convenient for patients
- Reduces side-effects

HEALTHCARE

- Improves adherence
- Enhances treatment efficacy

PAYERS

- Reduces clinic visits
- More cost-effective treatment

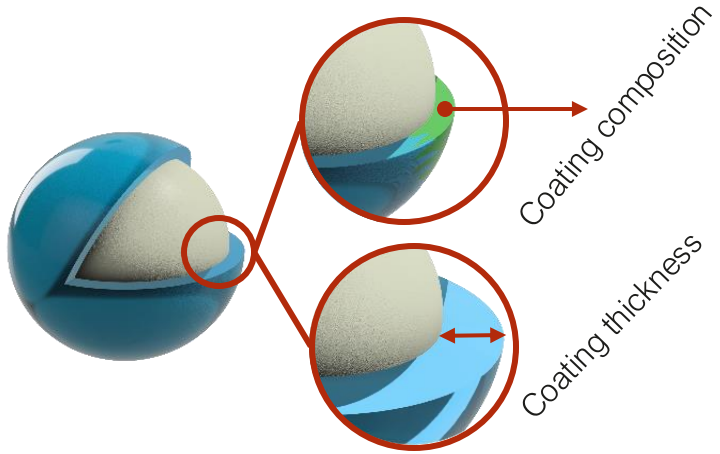
SUSTAINABILITY

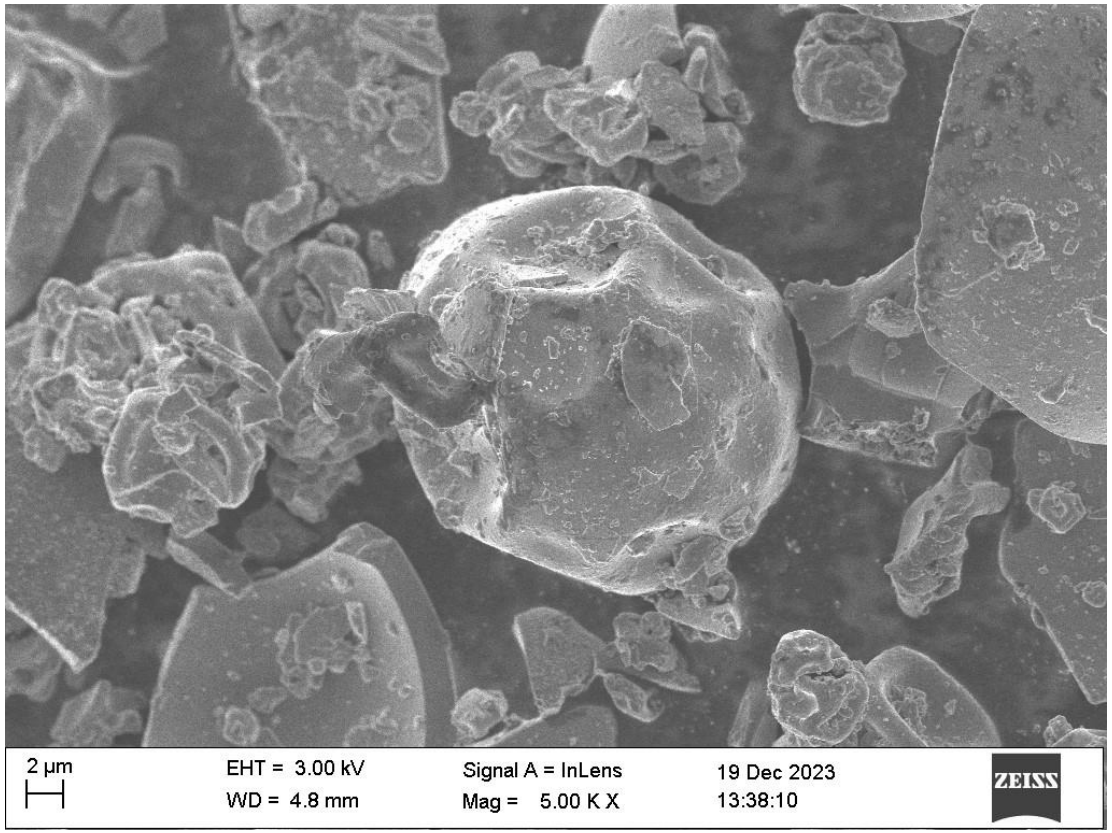
- Fewer injection devices, reducing environmental impact

PharmaShell®

Controls the duration of long acting injectables

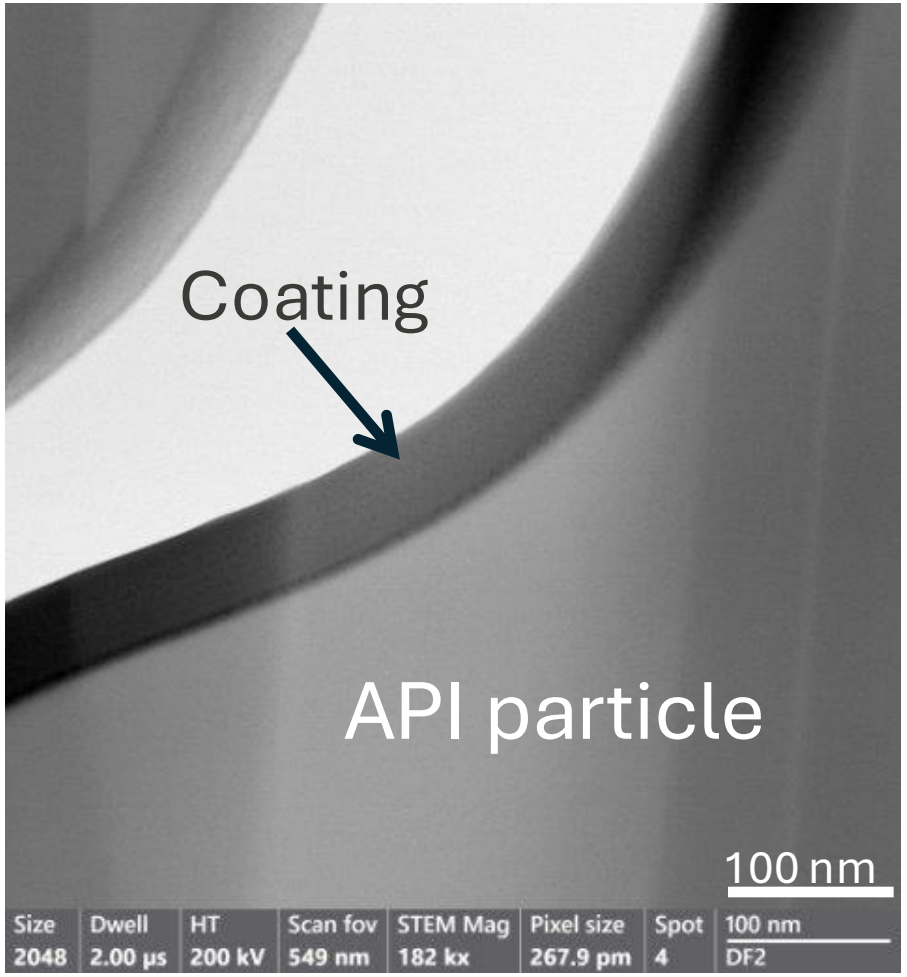
- The dissolution of the PharmaShell® coating controls the duration of the API release, up to several months, regardless of the API's half-life
- The release-profile can be tailored by adjusting coating composition and thickness
- Technology can be used with most APIs, especially suitable for biologics





PharmaShell® technology

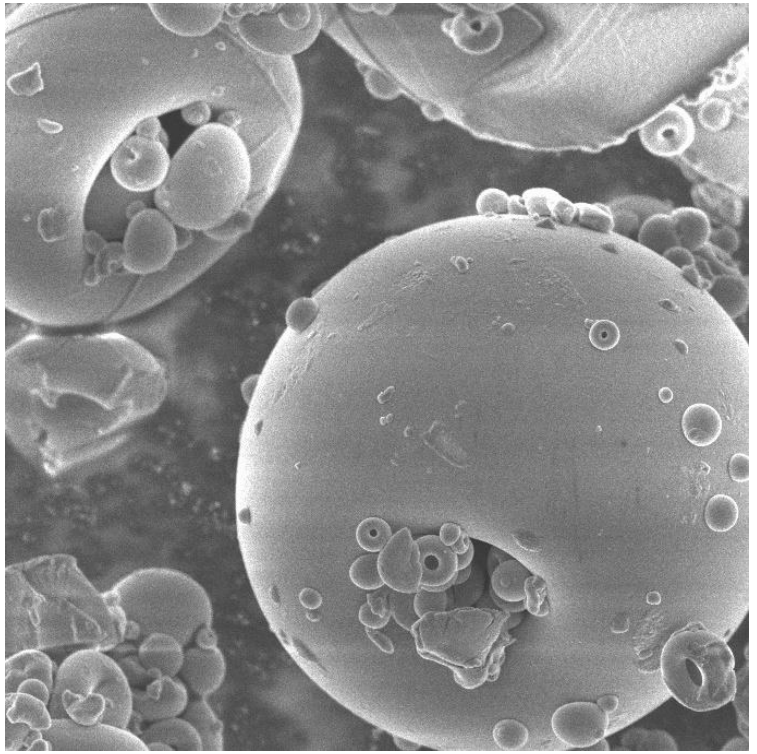
- Very dense and uniform over the particle
- Low permeability of liquids and gases and thereby protects the API



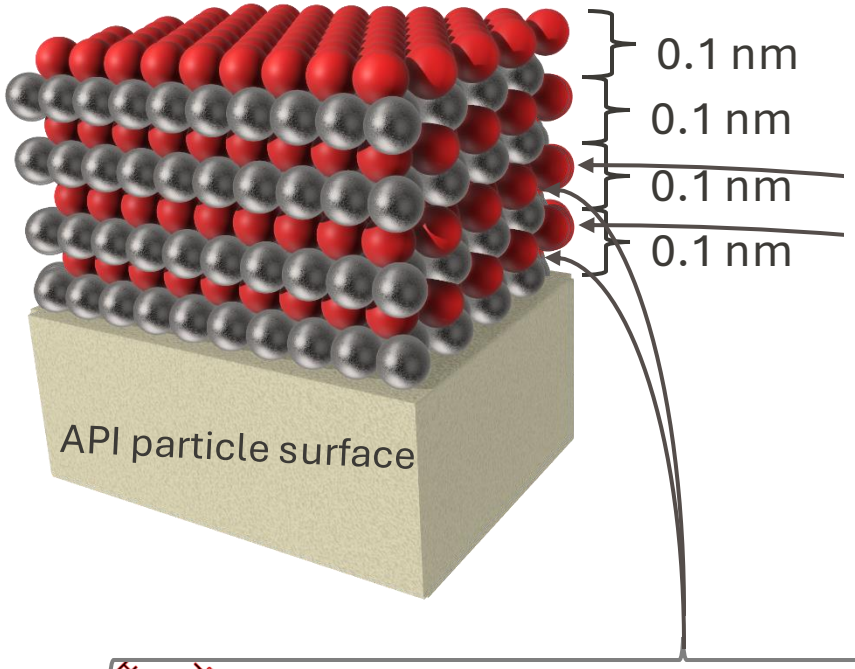
TEM image of coated particle

PharmaShell® by Atomic Layer Deposition

- ALD is a gas phase technique to coat surfaces
- Operates at low temperatures (near RT) and is a dry process
- Coating thickness in the nanometer range allows for a very high drug load
- Excellent process control enables tailoring of depot length and release profile by adjusting the ALD parameters such as composition and thickness
- No post-process purification steps needed



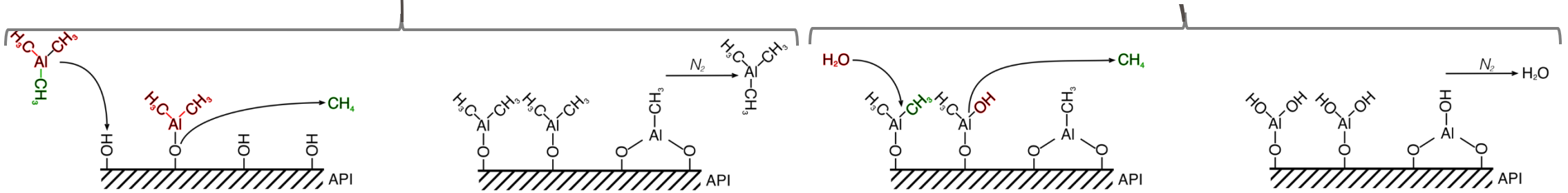
Atomic Layer Deposition (ALD)



- ALD's precision and repeatability come from separating and controlling when and where reactions occur.
- Reactions are separated in time to build the coating.

Example:

1. Metal reagent reacts on the surface.
2. Metal reagent-covered surface reacts with water to form metal oxide.
3. Reactions are cycled to ensure uniform coating.



Formulated to minimize injection pain

- **Thin Gauge Needles (30 G):** Ensures painless self-administration, improving patient comfort.
- **Low injection volume (<1 mL):** The ultra-high drug load enables low injection volumes, enhancing patient comfort.
- **Isotonic Solution:** Maintains osmotic balance, reducing discomfort during injection.
- **Physiological pH:** Matches the body's natural pH, minimizing irritation and pain.

19 G needle
E.g. Buvidal® and Zyprexa® Relprevv™

21 G needle
E.g. Uzedy® and Risperdal Consta®

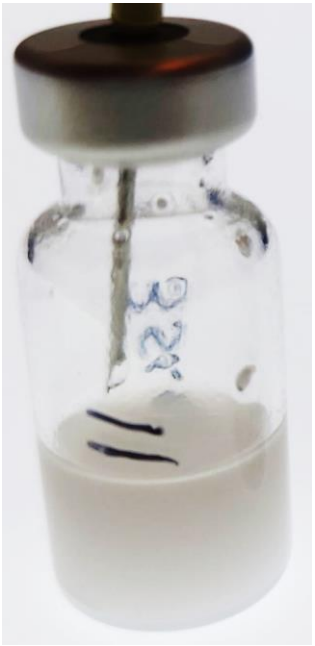
23 G needle
E.g. Abilify Maintena® and Invega Sustenna®

30 G needle
NEX-22

PharmaShell®

Liquids for suspension

- **One-compartment syringe systems:** Several options have been evaluated
- **Storage stability:** High potential indicated by low solubility of formulation components in liquid for suspension (confirmation pending)
- **Redispersibility:** Excellent, confirmed
- **Injectability:** Remains uncompromised
- **In vivo pharmacokinetics:** No observed impact



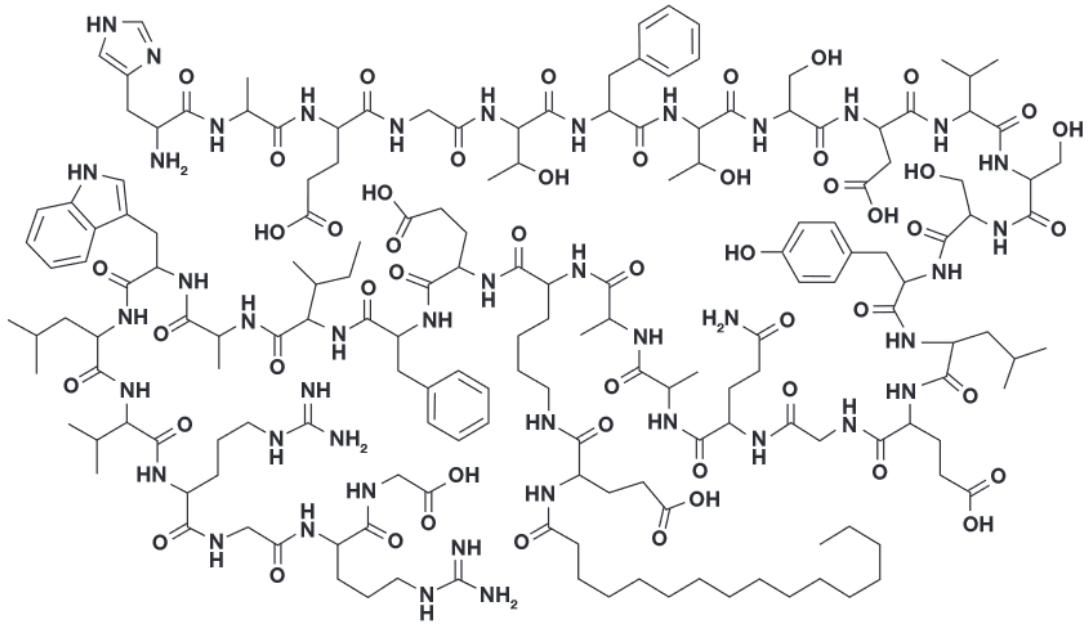
PharmaShell® system achievements
– more than 20 APIs coated

Nanexa internal projects

	Small molecules	Peptides	mAbs	NEX-22 *liraglutide*	NEX-20 *lenalidomide*	NEX-18 *azacitidine*	Partner projects
Prolonged release in vitro	✓	✓	✓	✓	✓	✓	✓
Controlled release in preclinical study	✓	✓	(✓)	✓	✓	✓	✓
Receptor affinity after PharmaShell process			✓				✓
Preclinical efficacy studies	✓						✓
Controlled release in in clinical study	✓	✓		✓	✓	✓	
Long term stability data	✓	✓	✓	✓	✓	✓	✓

NEX-22 (liraglutide)

- Once monthly (Q1M) s.c. administration for the treatment of type 2 diabetes
- GLP-1 analogue, 3.7 kDa
  - Binds to GLP-1-receptor, stimulates blood glucose dependant insulin secretion and suppresses glucagon secretion
- API currently approved as once-daily (Q1D) s.c. injectable (RLD Victoza®)



H-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys(γ-Glu-palmitoyl)-Glu-Phe-Ile-Ala-Trp-Leu-Val-Arg-Gly-Arg-Gly-OH

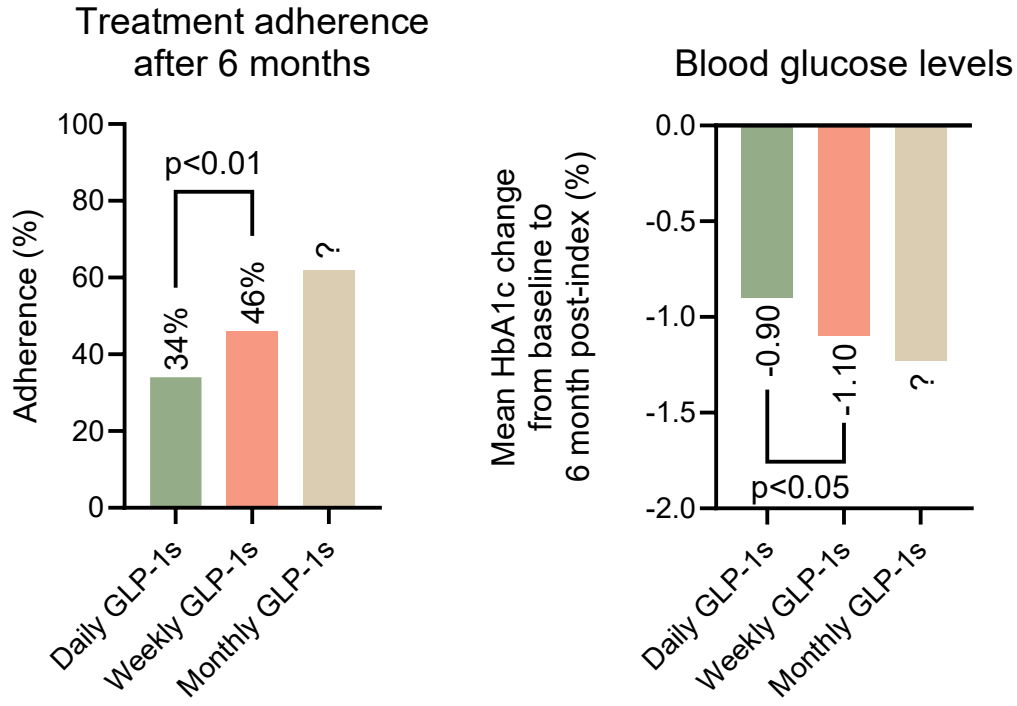
Long Acting Injectables Improving Adherence
—More Effective Outcomes for GLP-1 Treatment

Conclusions from US Clinical Practice (STAY Study)

- **Significantly Greater Adherence:** Weekly GLP-1 treatments show significantly higher adherence compared to daily treatments.
- **Improved Glycemic Control**: Weekly GLP-1 treatments result in a greater reduction in Glycated Hemoglobin (HbA1c).
- **Clinical Benefits:** Increased adherence leads to clear clinical benefits.

Potential for One-Month Long-Acting GLP-1

- **Enhanced Adherence:** A one-month long-acting GLP-1 has the potential to further improve adherence.
- **Better Clinical Outcomes:** Improved adherence is expected to lead to better clinical outcomes.



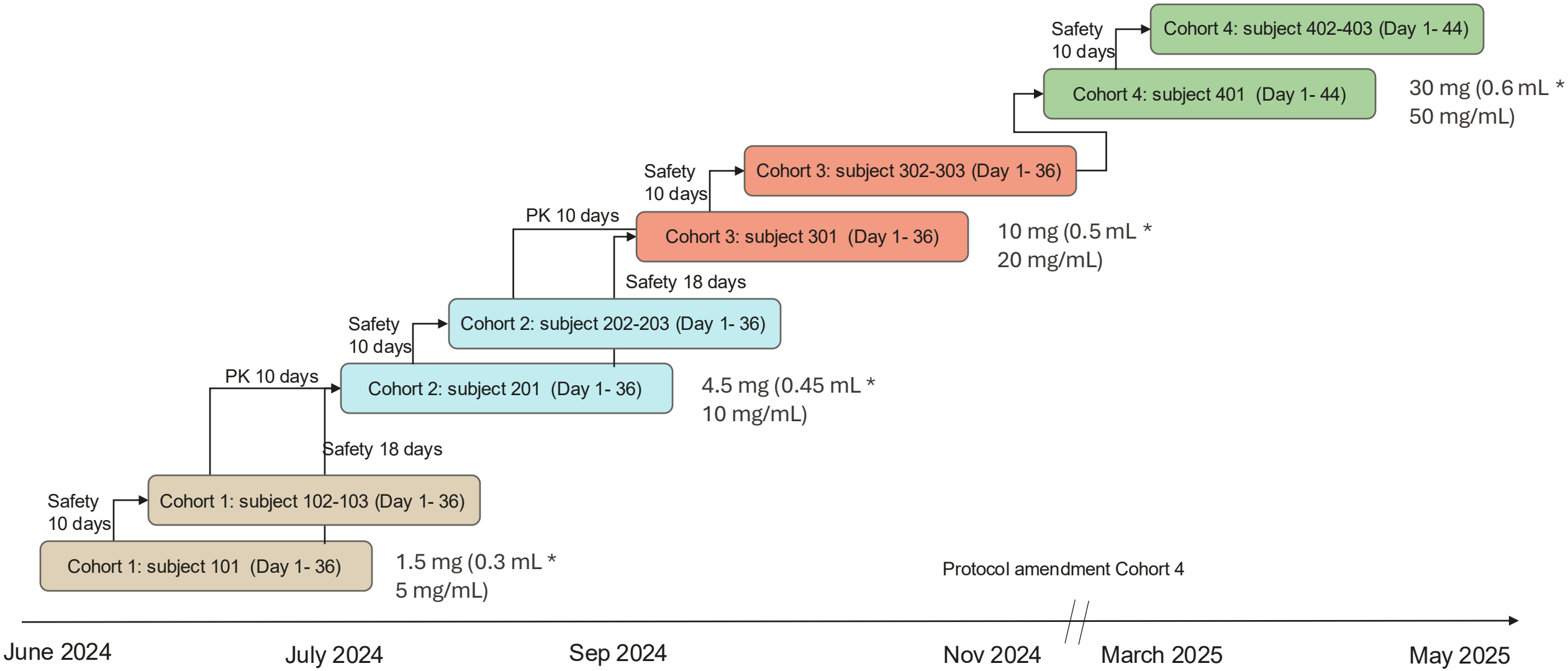
Adherence defined as proportion of days covered ≥ 80%

Polonsky et al. Diabetes Ther 13, 175–187 (2022) daily and weekly figures adapted from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8776963/figure/Fig3/

NEX-22 (liraglutide) Phase 1 study

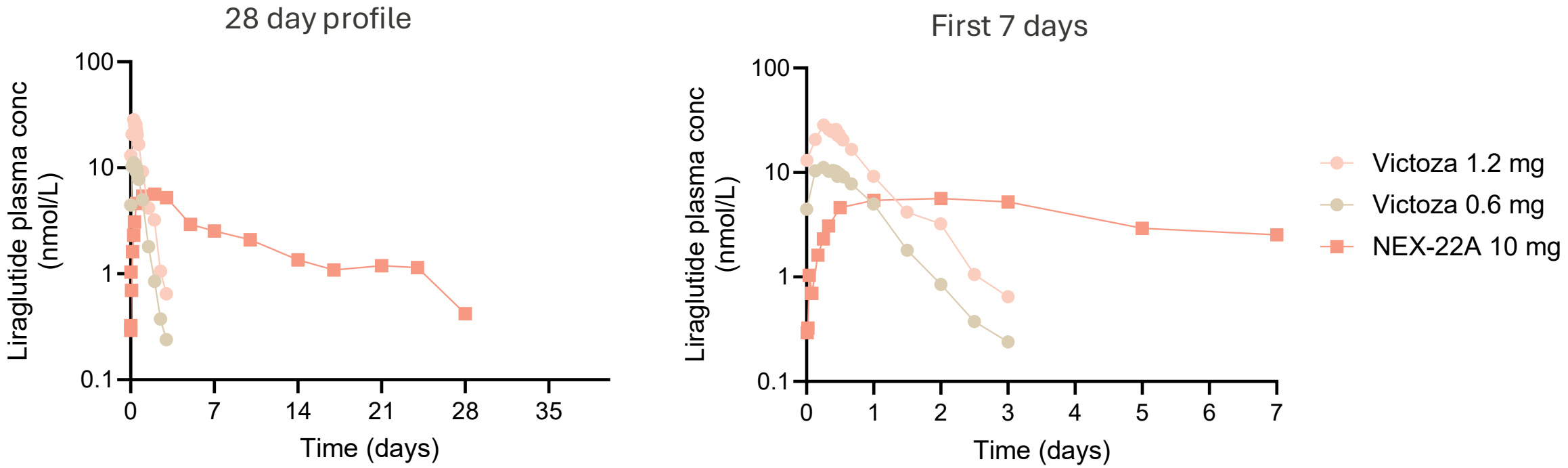
- Type 2 diabetes patients naive to GLP-1 treatment
- Single ascending dose study
  - Doses: 1.5 mg, 4.5 mg, 10 mg, and 30 mg
  - Concentrations: 5, 10, 20, and 50 mg/mL
  - Injection volume: 0.3–0.6 mL
- Primary objective: Pharmacokinetics
- Secondary objective: Safety and tolerability

NEX-22-01 Dose cohorts



NEX-22A Human PK

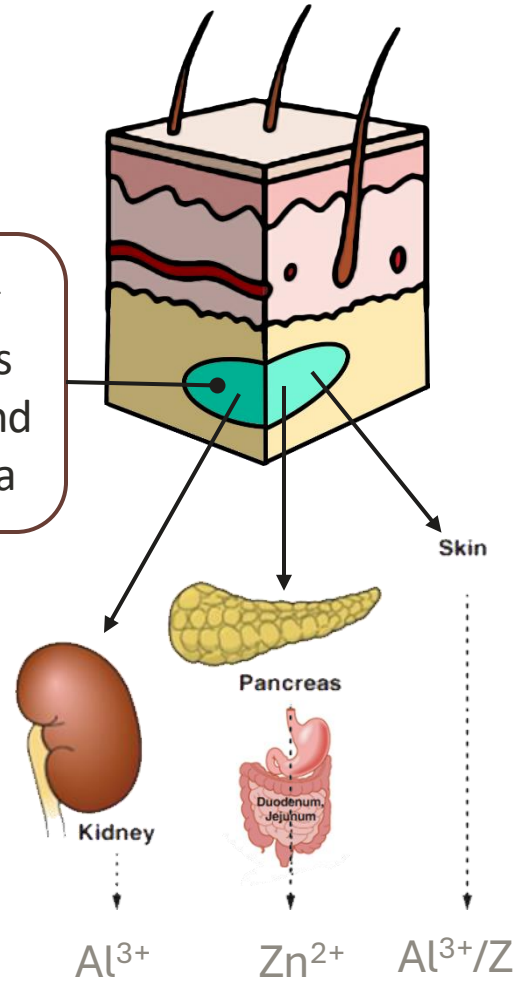
—Compared with RLD



NEX-22 interim data from NEX-22-01 Phase I study
Victoza data from DOI: 10.1007/s40262-015-0343-6

Elimination of PharmaShell® components

Zn^{2+} and Al^{3+} ions dissolves from depot and enters plasma



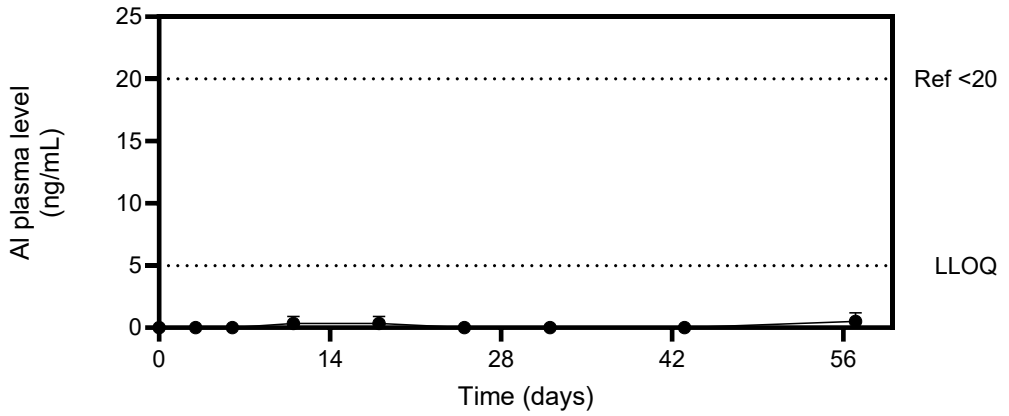
No risk for accumulation of zinc

Daily dose zinc from NEX-22 < 5% of a recommended daily intake

Low aluminium levels

Aluminium exposure does not exceed 5 µg/kg/day* and stays below 20 ng/mL reference threshold

Al plasma levels after administration of 30 mg NEX-22A in humans



* FDA-2022-D-2301: aluminium content in parenteral nutrition products

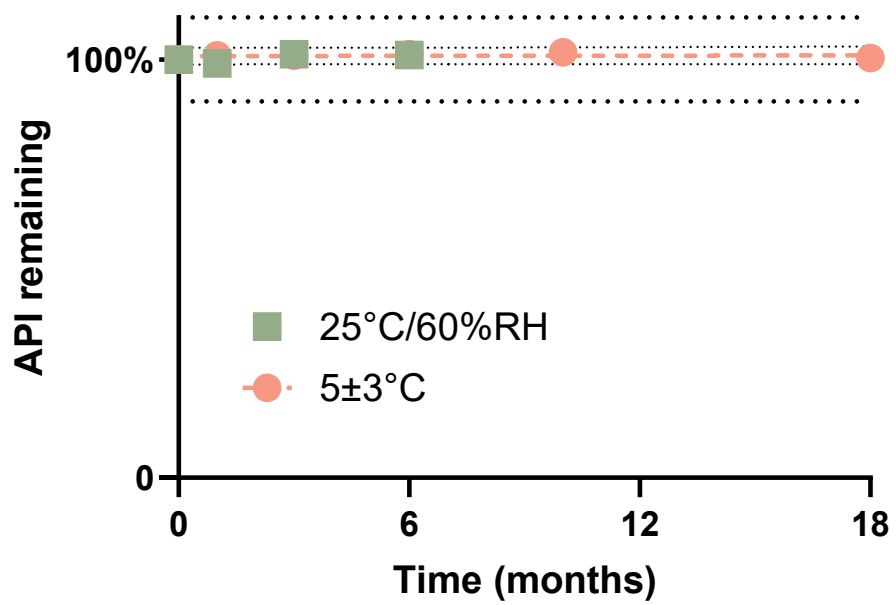
Outstanding stability (liraglutide)

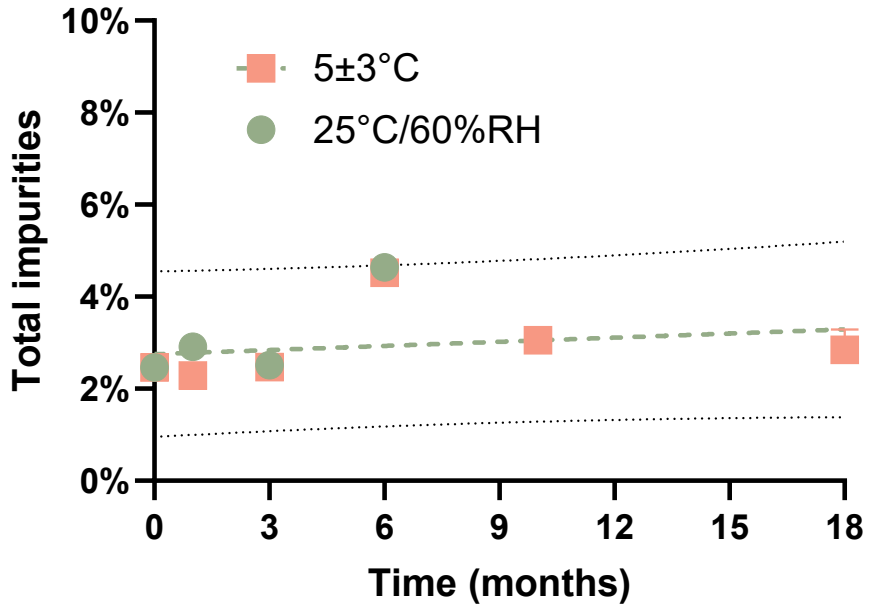
—PharmaShell® protects API during storage

- NEX-22 shows no difference between refrigerated and Zone II ambient storage conditions
  - Real-time data up to 6 mo in Zone II conditions
  - RLD: 30 mo in 5±3°C, 1 mo in 25–30 °C
- NEX-22 preserves product quality and efficacy without the need for cold storage requirements.

"Up to 30% of biologics' total costs come from cold chain logistics"

11th edition of the *Biopharma Cold Chain Sourcebook*, Pharmaceutical Commerce

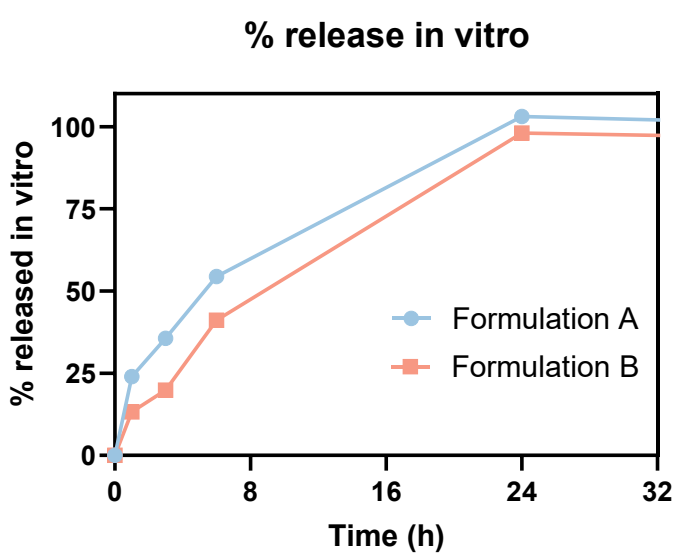


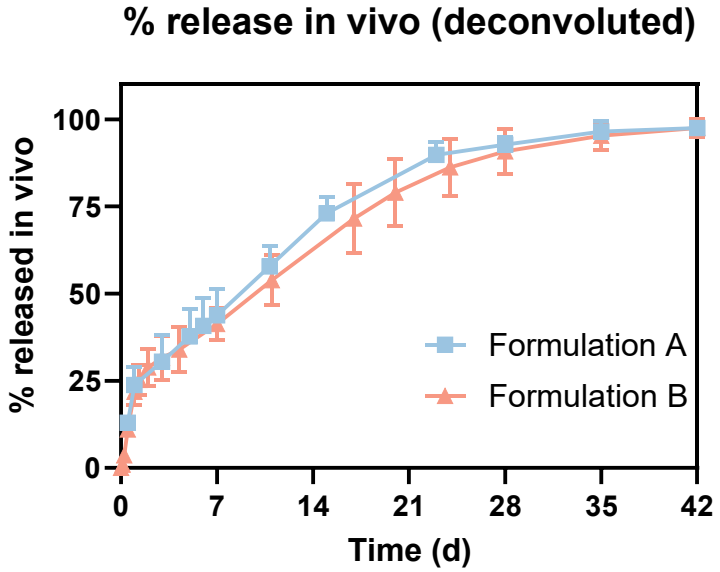


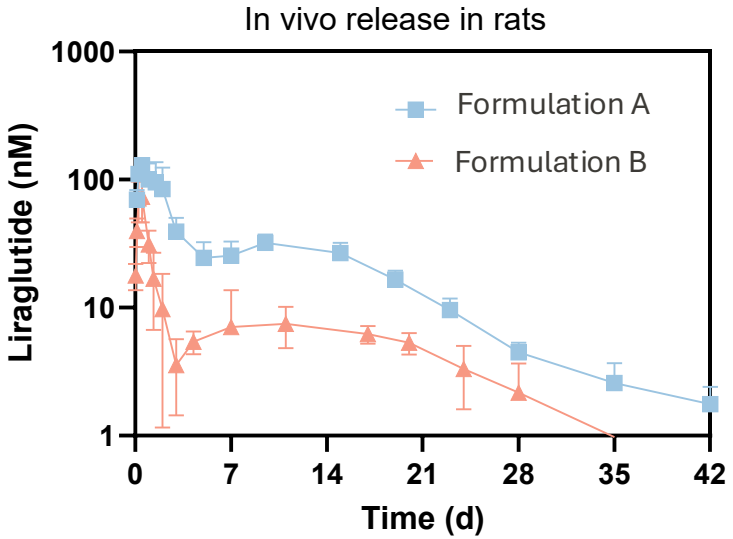
NEX-22 IVIVC

(*in vitro in vivo* correlation)

- Fundamental assumption: *in vitro* dissolution reflects the *in vivo* plasma profile.
  - Deconvolute the plasma profile using AUC0-t/AUCinf.
- Analyze and compare the deconvoluted plasma profiles with the *in vitro* dissolution profiles.



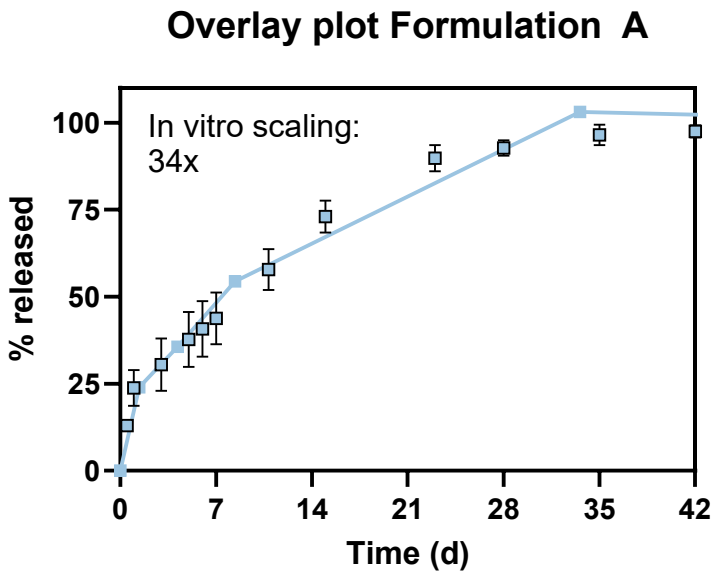


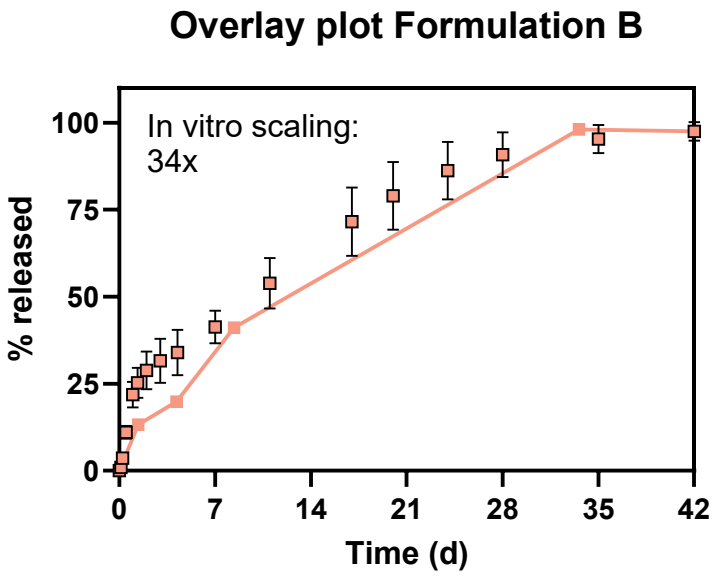


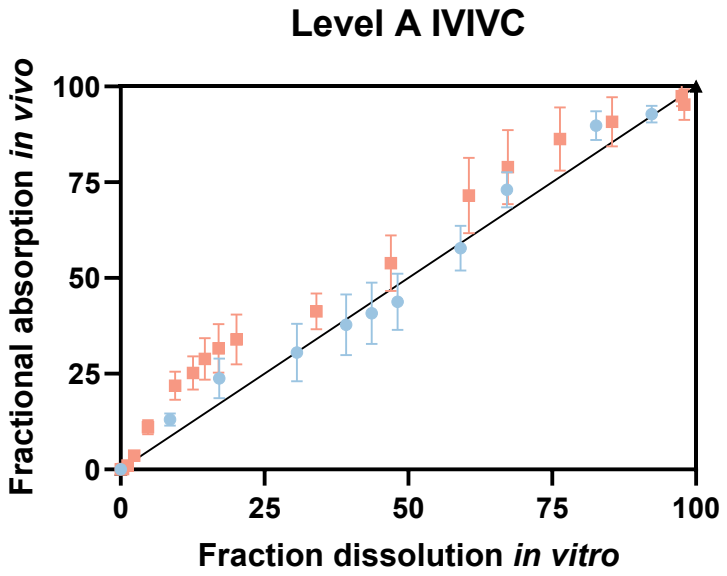
NEX-22 IVIVC (cont'd)

(*in vitro in vivo* correlation)

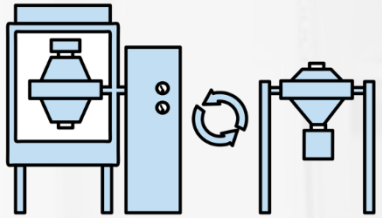
- Modify the time scaling factor until the *in vitro* release and the deconvoluted *in vivo* plasma profiles align closely.
- Implement the time-scaling factor on the *in vitro* dissolution profiles.
- Plot time-matched values from the time-scaled *in vitro* release curve (x-axis) and deconvoluted *in vivo* plasma profile (y-axis).







GMP manufacturing process



Gamma Sterilisation

Micronization | ALD & sieving | Bulk filling | Filling in cartridge | Sterilisation | Labelling, packing

CMO | Nanexa production facility | CMO

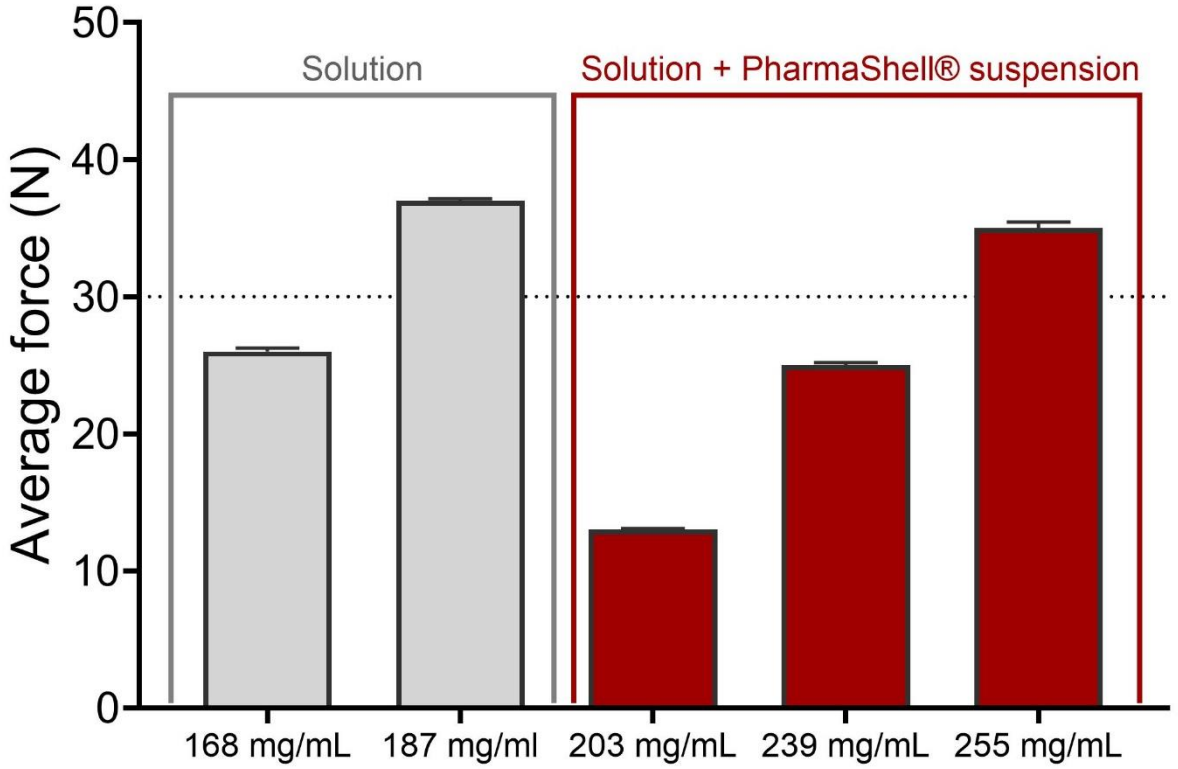
Liquid for suspension manufacturing | Labelling, packing

CMO | Nanexa

Antibody (mAb) formulation with PharmaShell®

—Reducing injection force by combining solution with coated microparticles (concept)

- Coated IgG1 mAb (60% protein, w/w, D_{50} 10 µm) was suspended in mAb-containing solution (30 mg/ml, red bars)
- Compared vs solution in His-NaAc buffer, pH 5.5
- 2-mL syringe, fitted with 26 G×13mm hypodermic needle, 180 µl/s (5.6 s/mL)
- Suspension in mAb solution vehicle facilitates ultra-high concentration delivery of API through narrow gauge needles

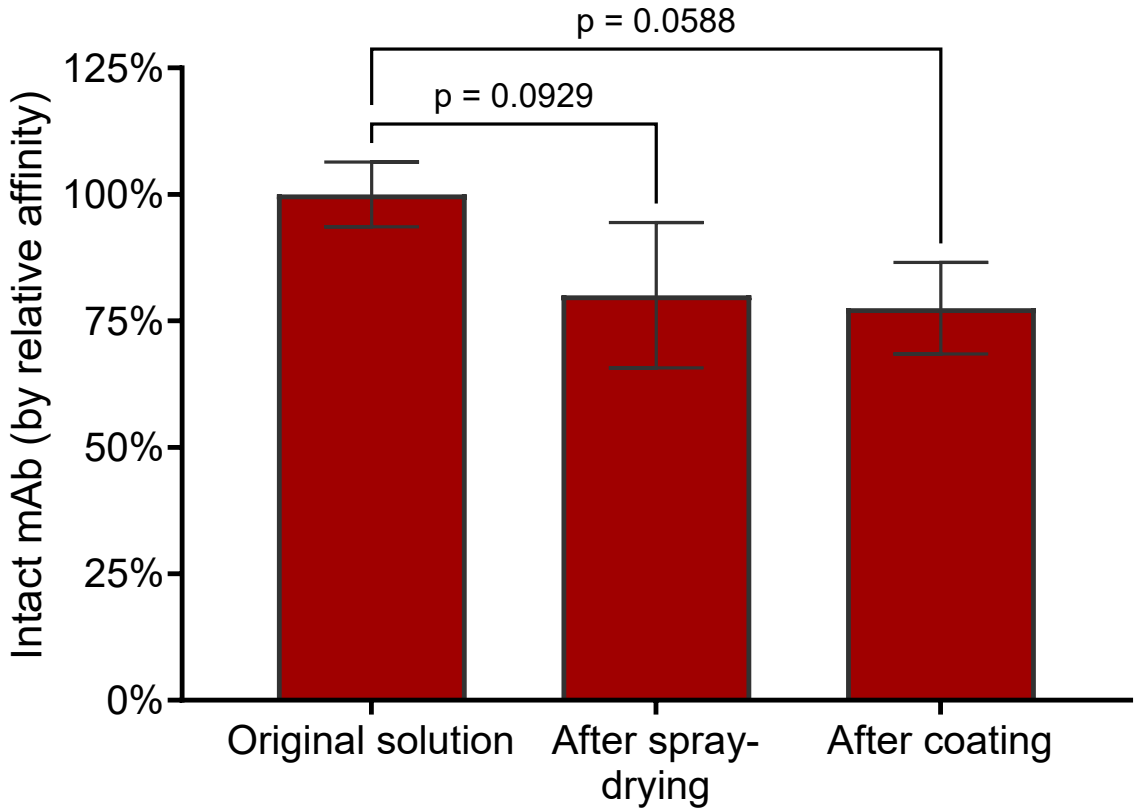


Source: Nanexa on file

Antibody (mAb) formulation with PharmaShell®

—Maintaining affinity after coating

- Affinity to the antigen was measured through enzymatic ligation assay (ELISA) and compared between processing steps
  - Solvent exchange
  - Spray-drying
  - PharmaShell®-coating
- Coated mAb was not significantly different from unprocessed mAb
- Disclaimer: Bioavailability may be reduced (inconclusive data)



PharmaShell®

Next-gen injectables with atomic layer precision

PharmaShell® key attributes

- ✓ **Controlled Onset and Release:** Provides quick and sustained efficacy for weeks to months.
- ✓ **Ultra-High Drug Load:** Allows for low injection volumes, enhancing patient comfort.
- ✓ **Versatile:** PharmaShell® technology can control the release of any API. The half-life of the API is irrelevant. No changes to the API structure are needed.
- ✓ **Ease of Administration:** Simple and convenient for users.
- ✓ **Outstanding Stability:** Eliminates the need for cold-chain.

Thank you for listening!

Do you want to know more or initiate partner discussions?

Reach out to:
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Dr. Oliver Hedge, oliver.hedge@nanexa.se